NIH fMRI Summer course

Computational modeling and fMRI

(2nd order statistics, across-trial variability and trajectory-based processing)

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National Institutes of Health

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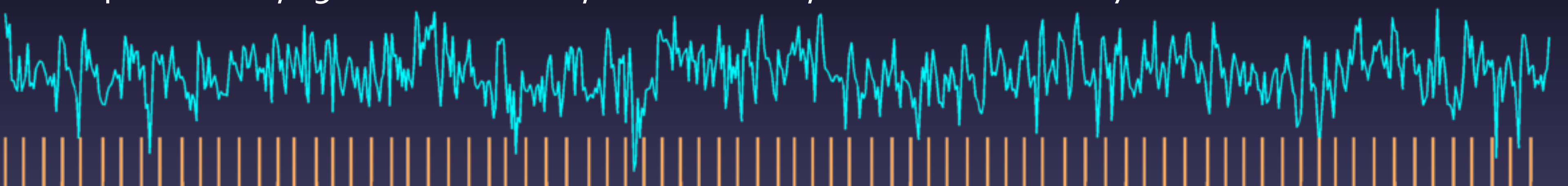
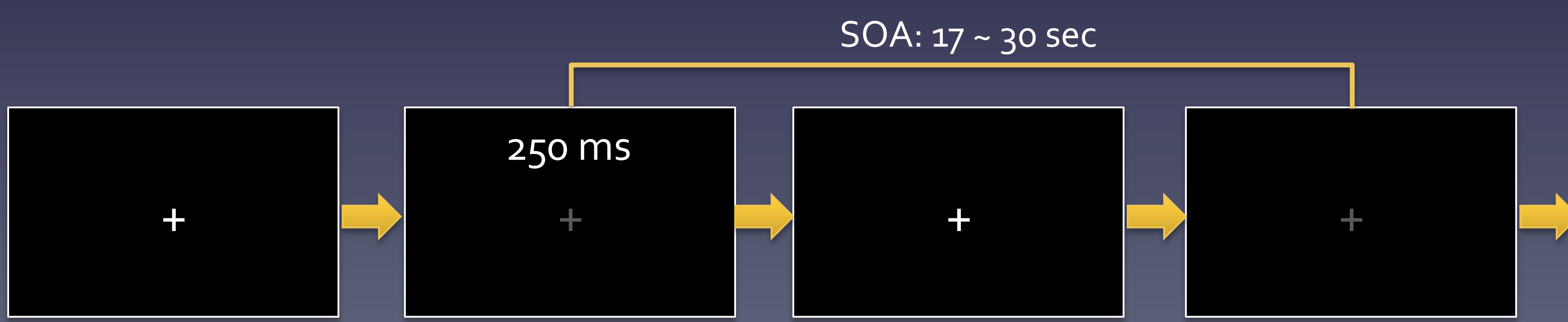
Talk Outline

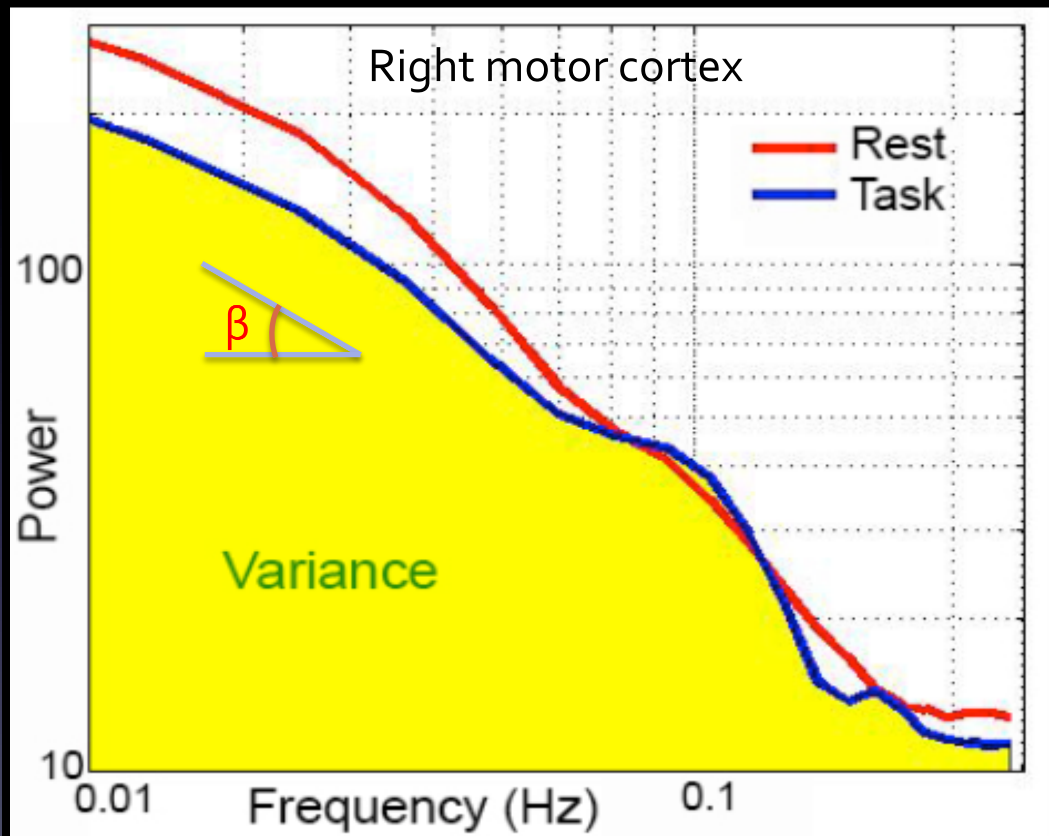
- 2^{nd}-order statistics of fMRI signal
  - <u>1^{st} order</u>: mean
  - <u>2^{nd} order</u>: variance; power spectrum; auto-correlation
- The relation between ongoing and evoked activity
  - How to assess
  - An example of overwhelming negative interaction in fMRI
- Trajectory-based processing
  - A more parsimonious and realistic model
- Similar observations in electrophysiology

Subject #1, right motor cortex (RMC), resting-state
4 fMRI runs, 190 volumes each, TR = 2.16 sec, total scan time ~27 min

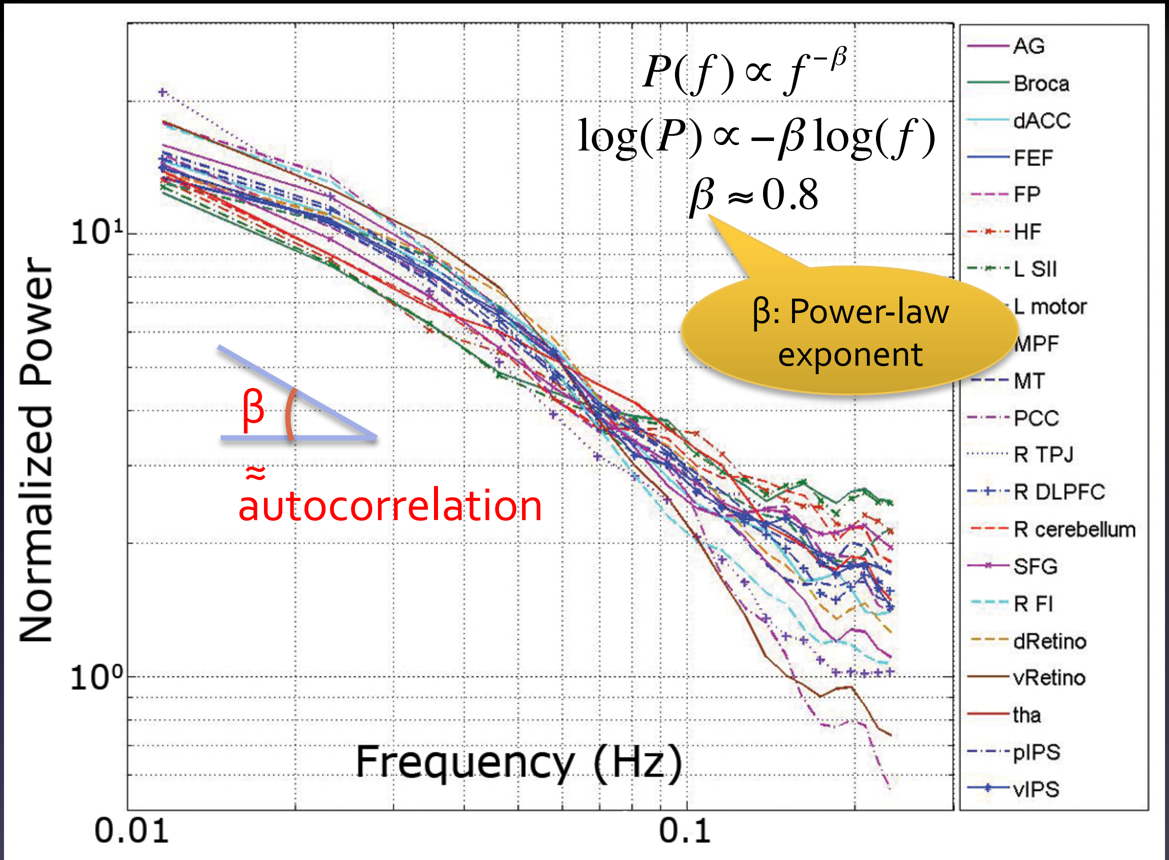
Subject #1, right motor cortex (RMC), visual detection task (80 trials total)
4 fMRI runs, 190 volumes each, TR = 2.16 sec, total scan time ~27 min





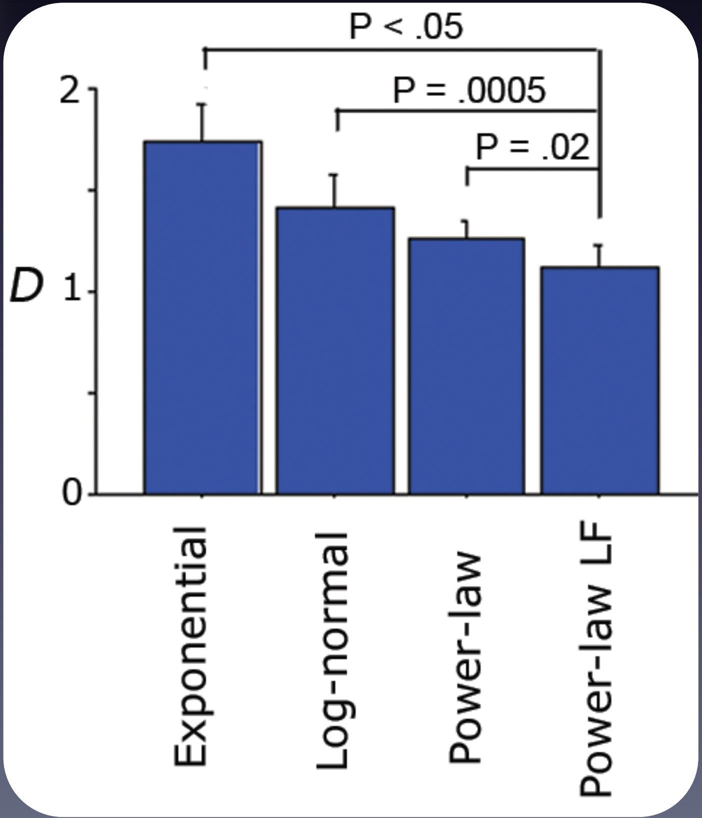

Right motor cortex
Rest
Task
100
10
Power
β
Variance
0.01
Frequency (Hz)
0.1

fMRI signal temporal power spectra



If 0 < β < 1, autocorrelation function follows:

$$r \propto 1/\tau^{1-\beta} \propto \tau^{-(1-\beta)}$$



He, JNS 2011

Scale invariance; scale-free;

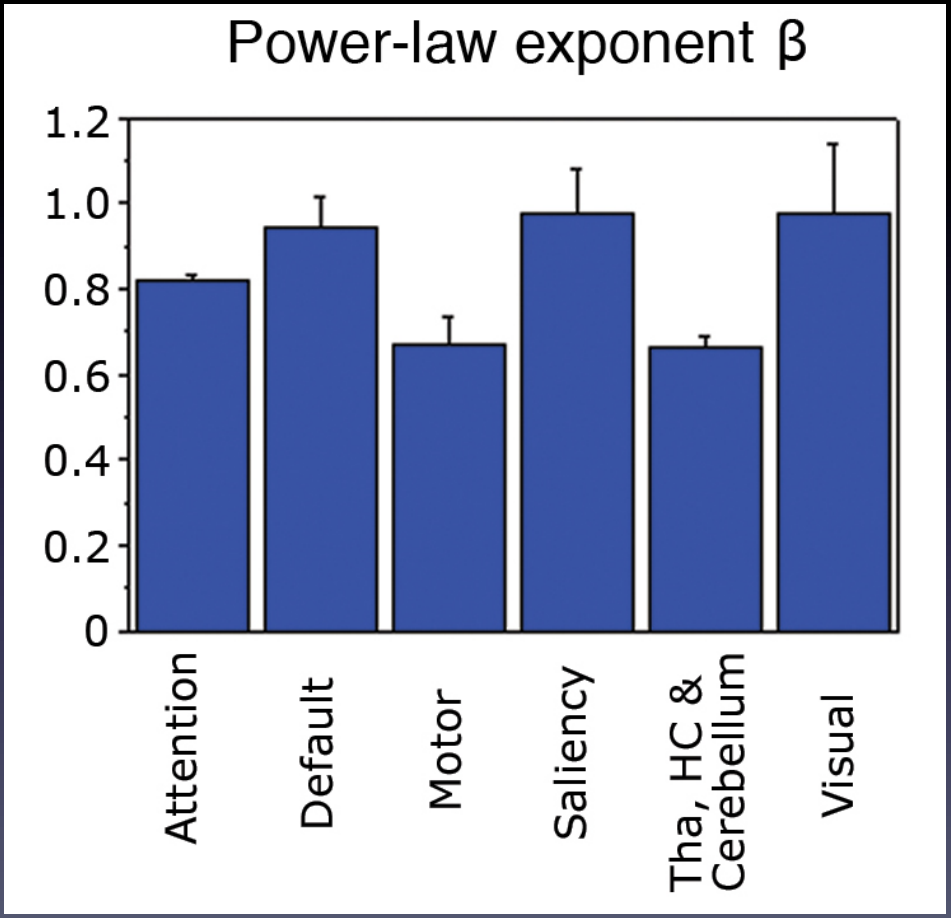
$$f(\lambda x) =_d \lambda^H f(x)$$

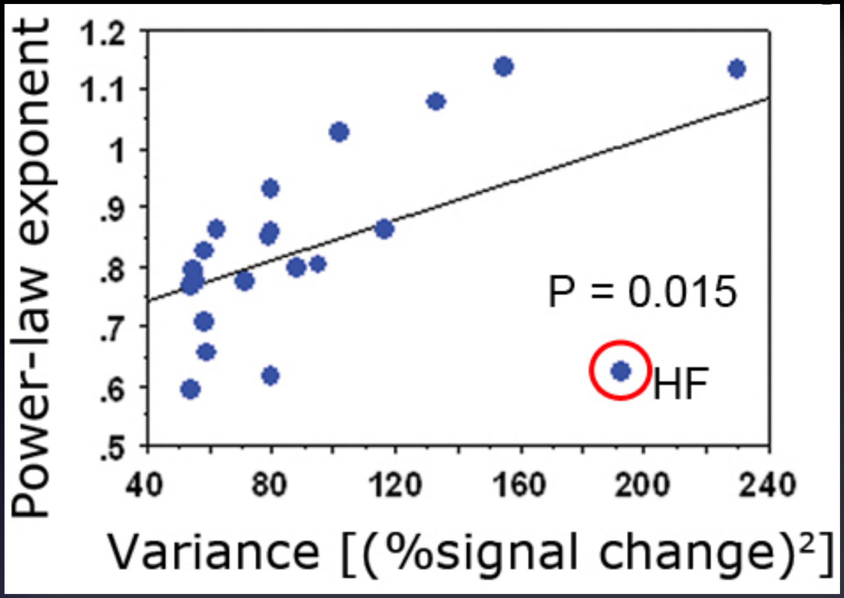
Temporal domain: Scale-free dynamics;
Spatial domain: Fractals

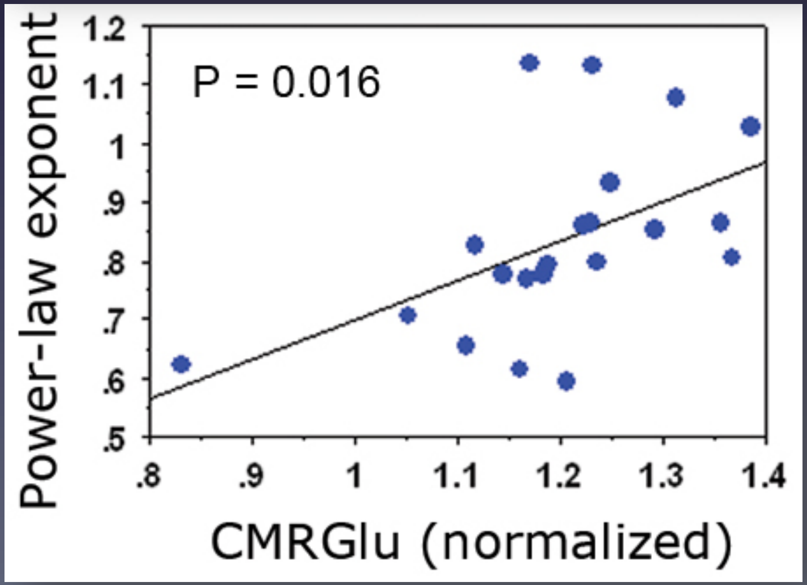
If $P(f) = Af^{-\beta}$

Then $P(\lambda f) = A(\lambda f)^{-\beta} = A\lambda^{-\beta} f^{-\beta} = \lambda^{-\beta} P(f)$

Power-law exponent differentiates between brain networks and correlates with metabolism

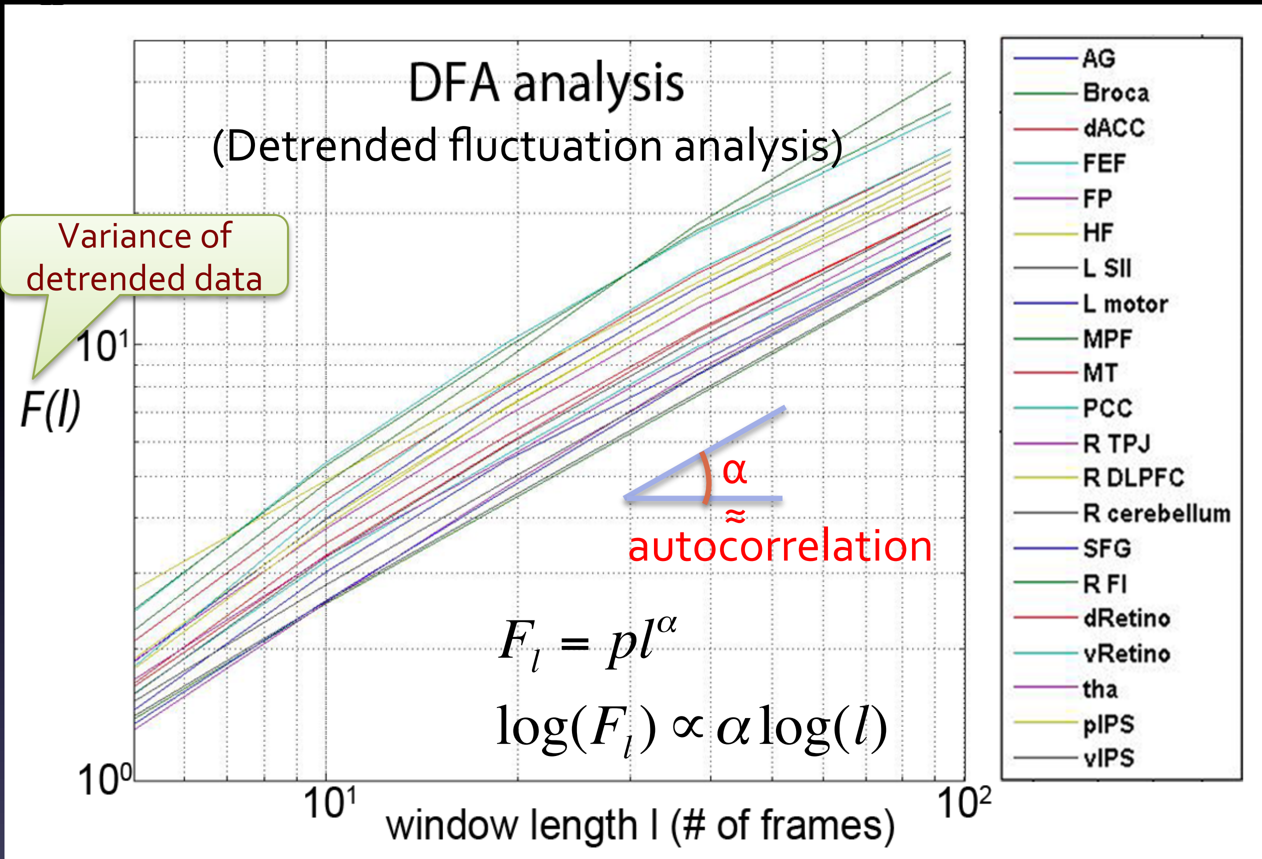






He, JNS 2011

Time-domain scaling analysis

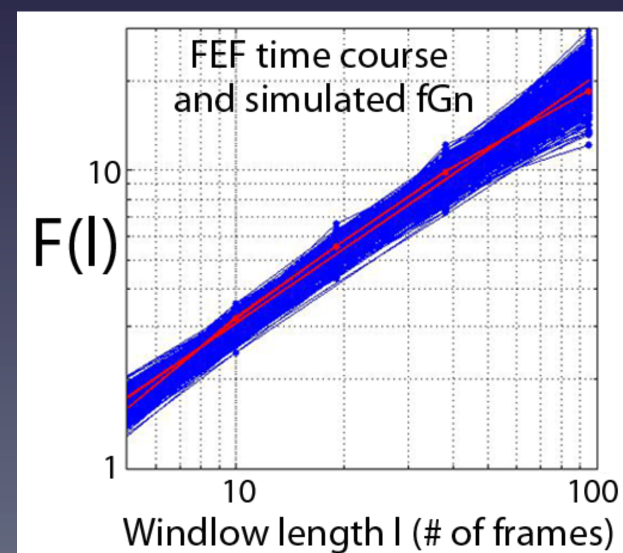


Scale-invariance:

$$f(\lambda x) =_d \lambda^H f(x)$$

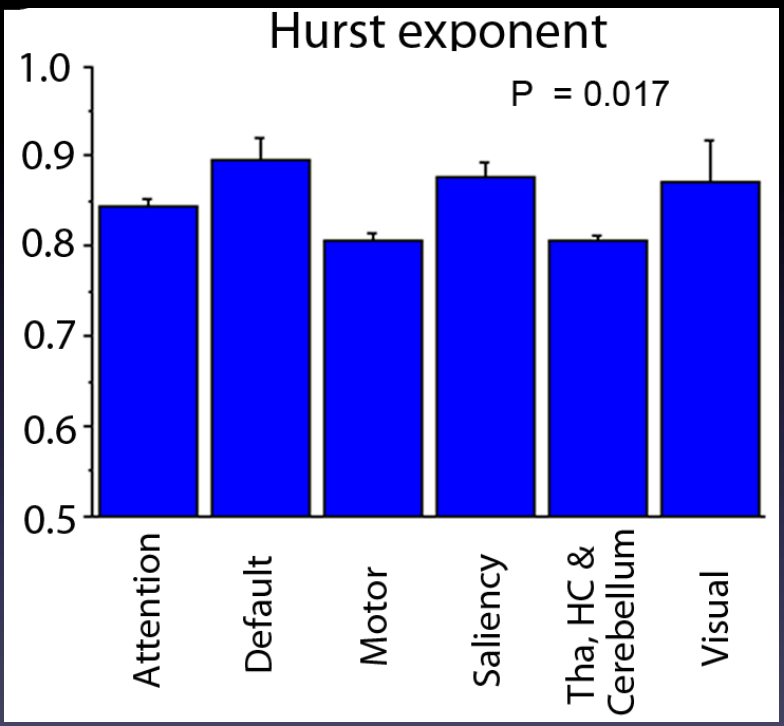
If α < 1,
Hurst exponent
H = α;

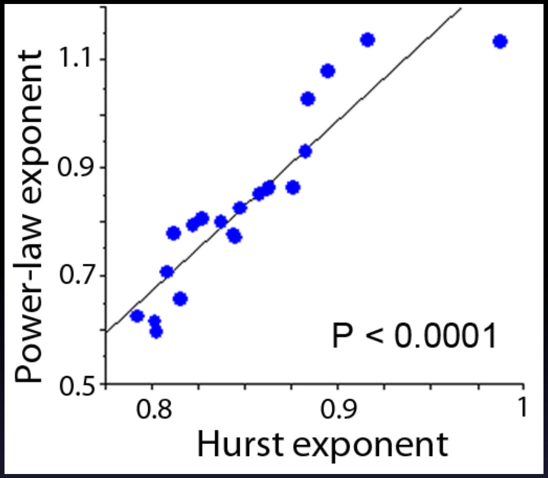
Goodness-of-fit test

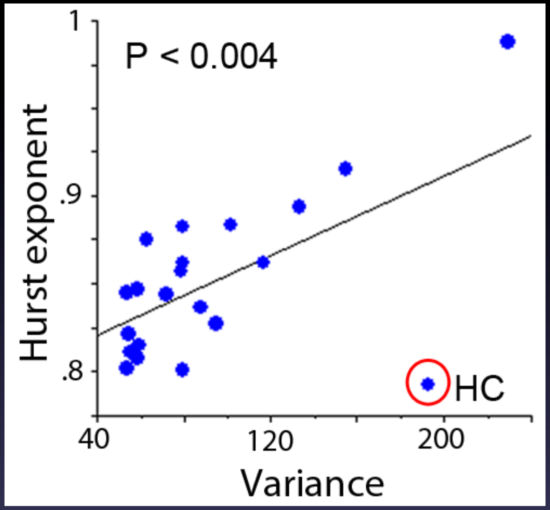


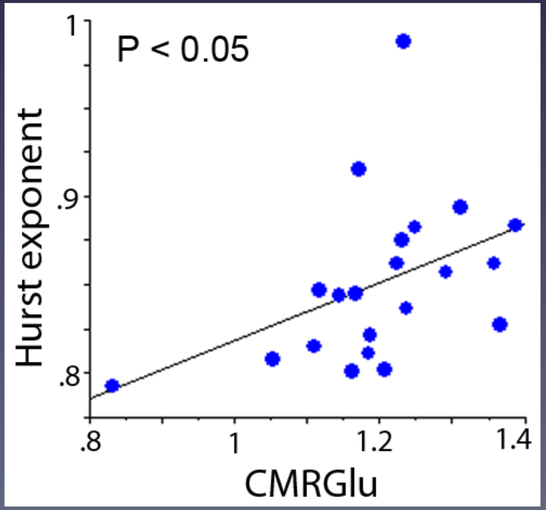
He, JNS 2011

Hurst exponent reproduces results from power-law exponent



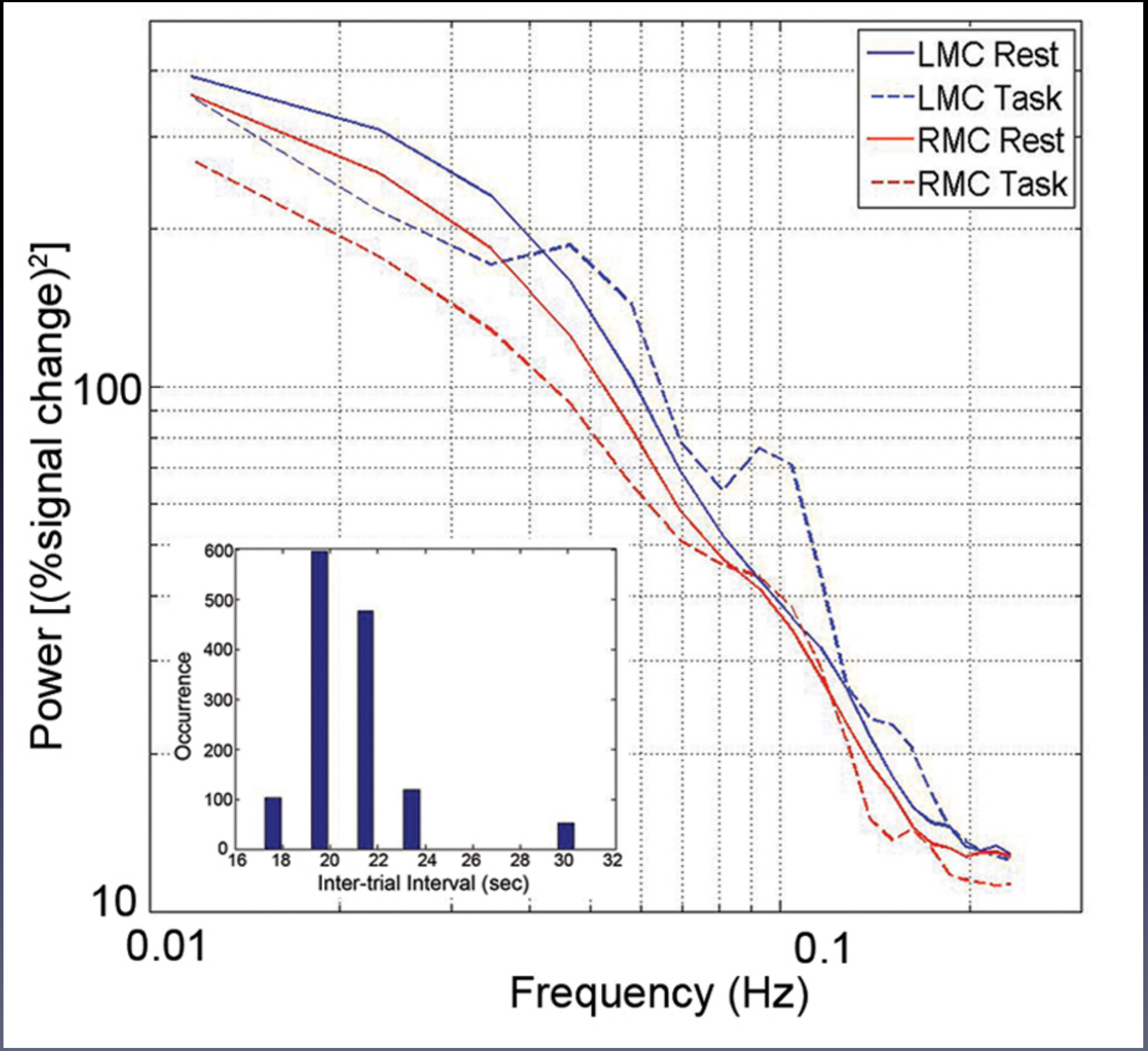






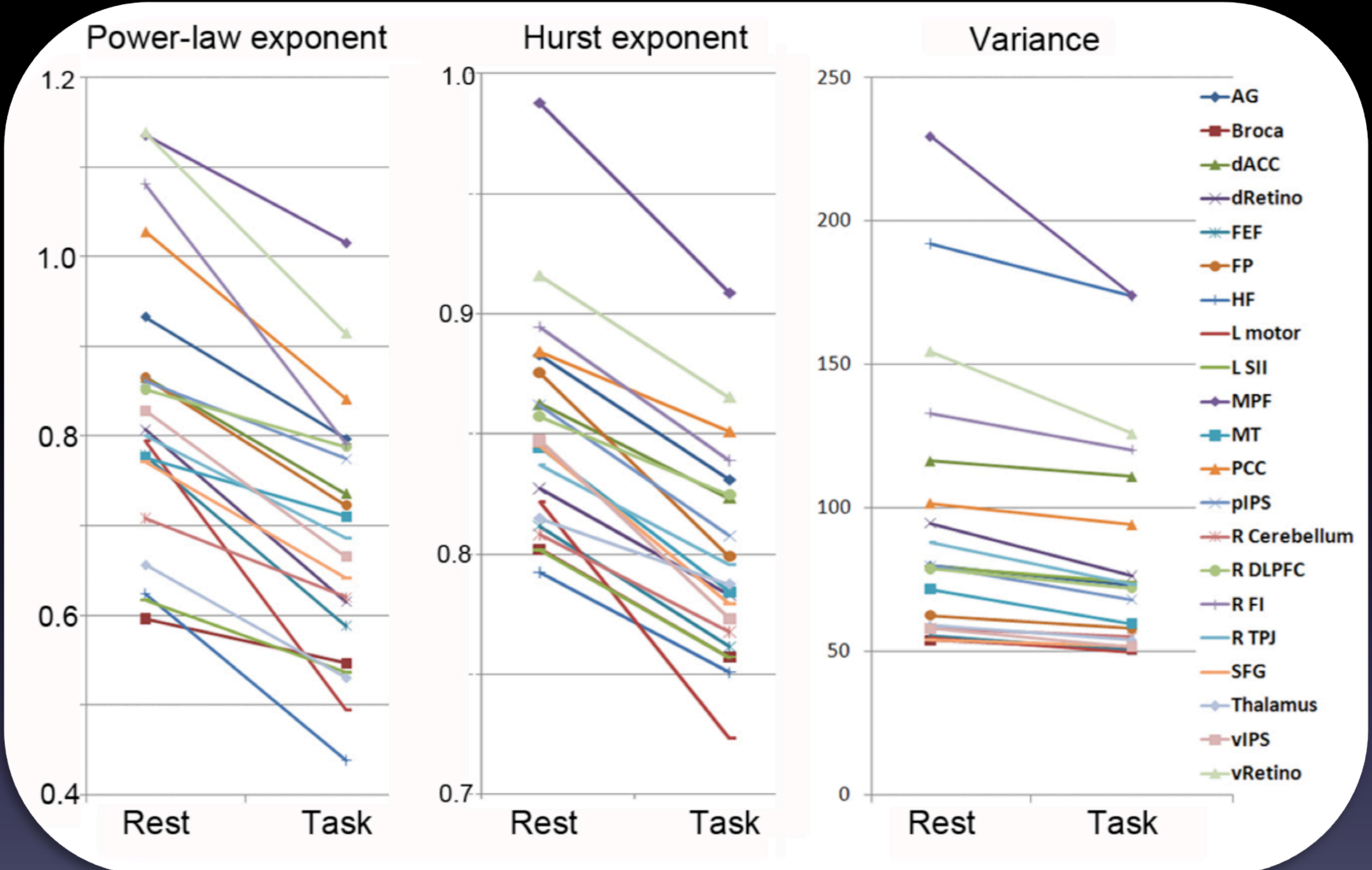
He, JNS 2011

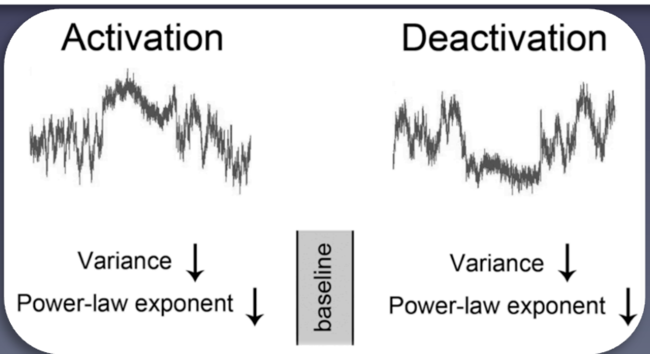
Power-law exponent decreases during task



He, JNS 2011

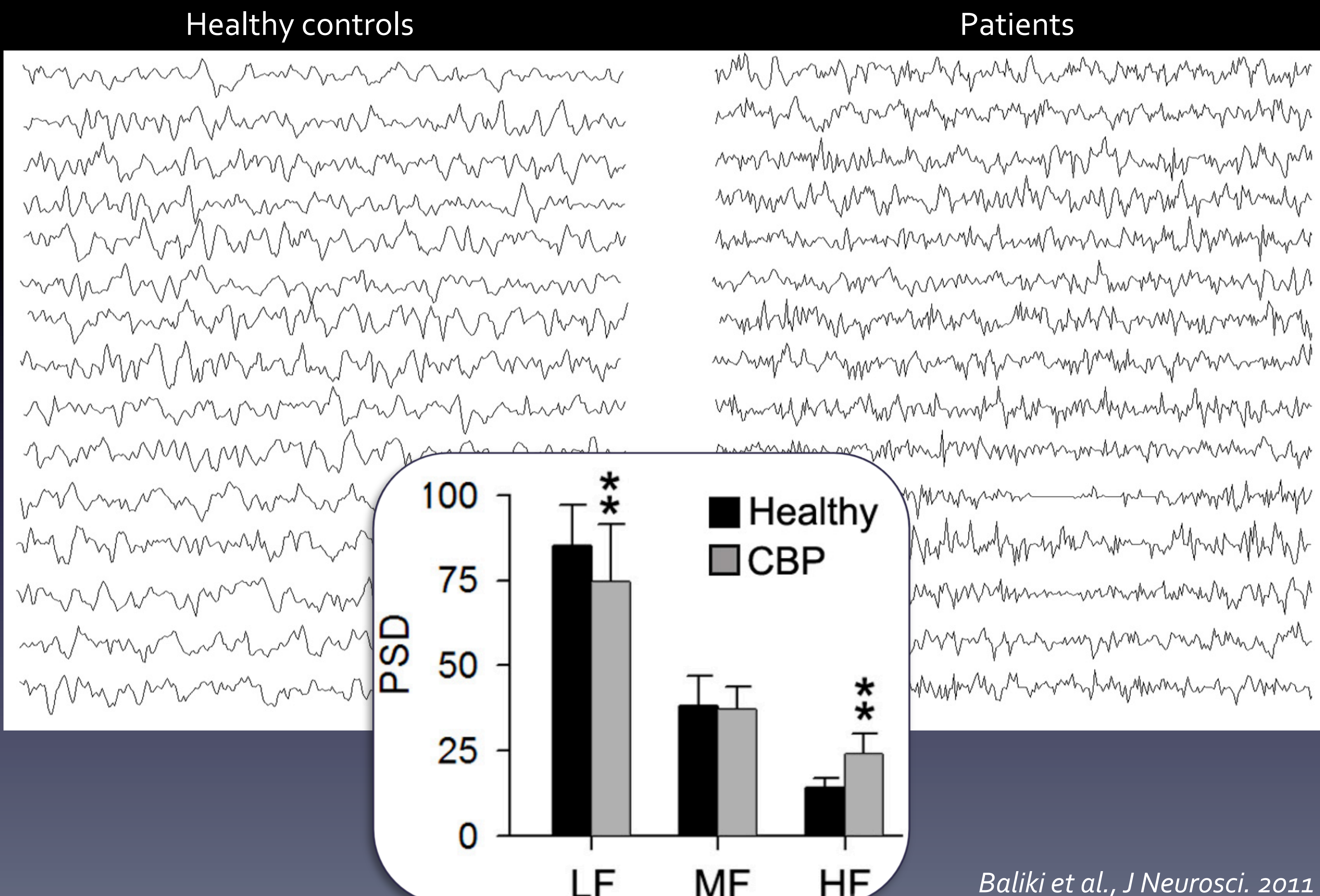
Widespread changes in scaling behavior during task





He, JNS 2011

Potential clinical applications - Chronic back pain

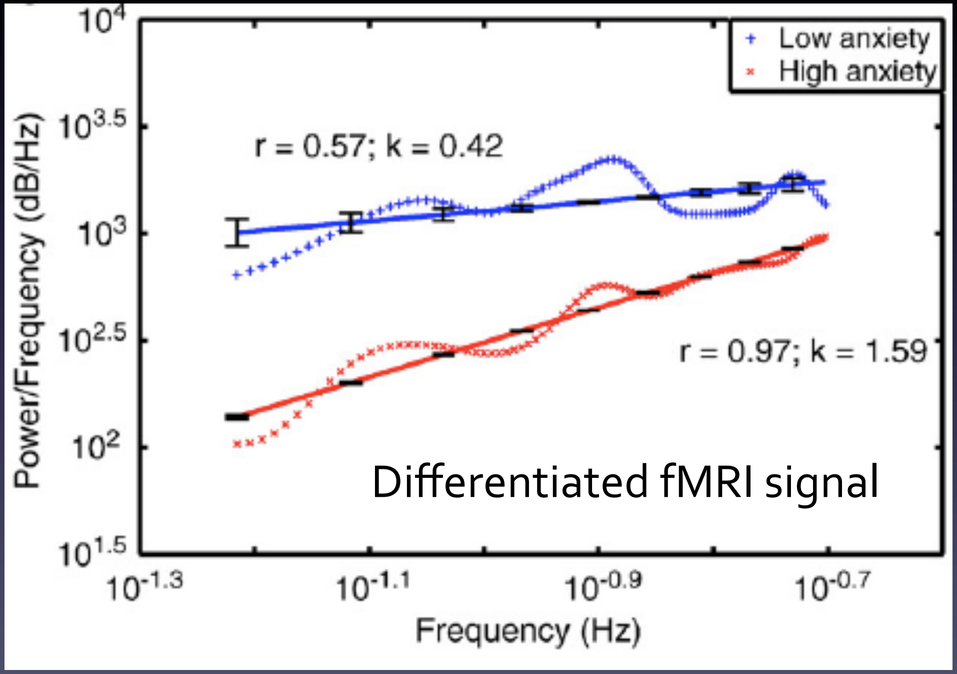


Baliki et al., J Neurosci. 2011

Potential clinical applications

Trait anxiety

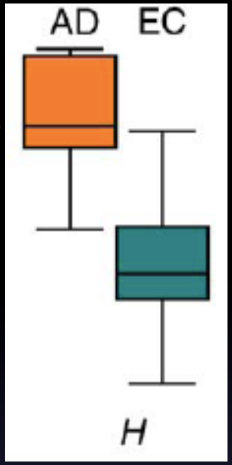
Smaller H → higher anxiety
Brain being constantly activated?

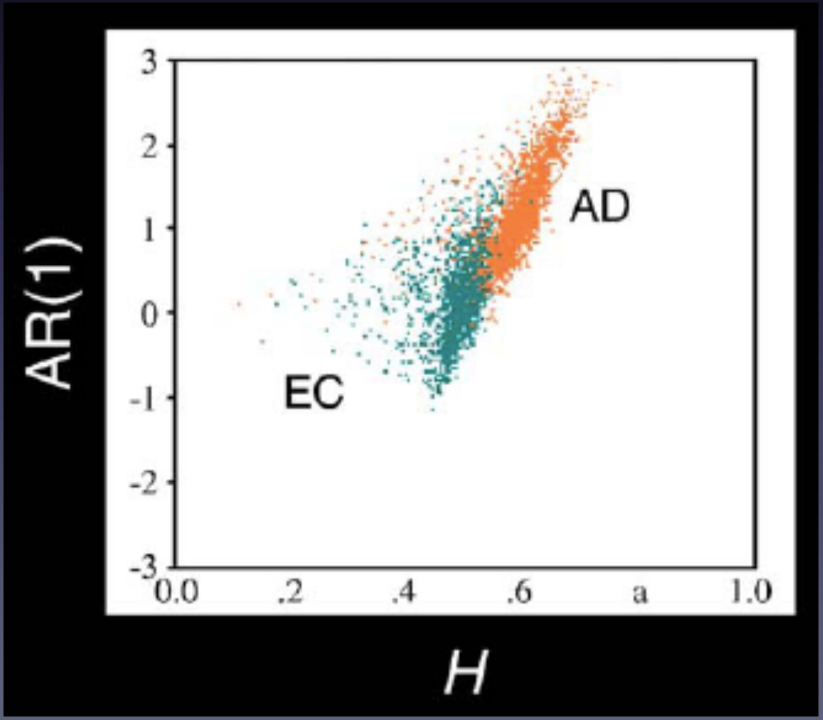


Tulkonov et al., 2010

Alzheimer's Disease

Larger H – AD
Not as efficient in online information processing?





Maxim et al., 2005

Interim Summary

2nd-order statistics of fMRI signal (variance; power-law exponent; autocorrelation)

- Differentiates between brain networks
- Correlates with brain metabolism
- Reduced variance and temporal memory/redundancy during task performance
- Mean-and-variance stationary; contains an optimal dynamic range

Talk Outline

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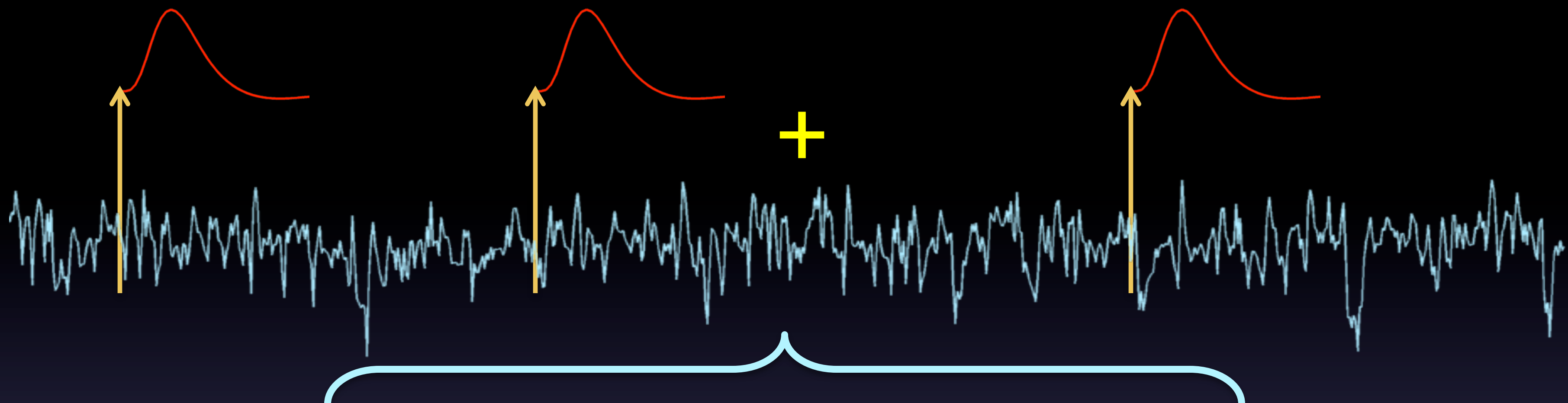
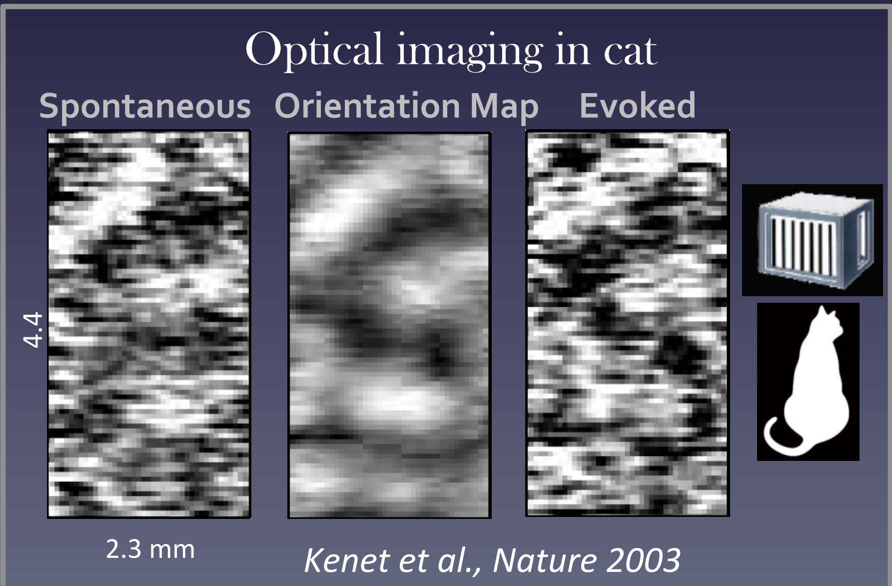
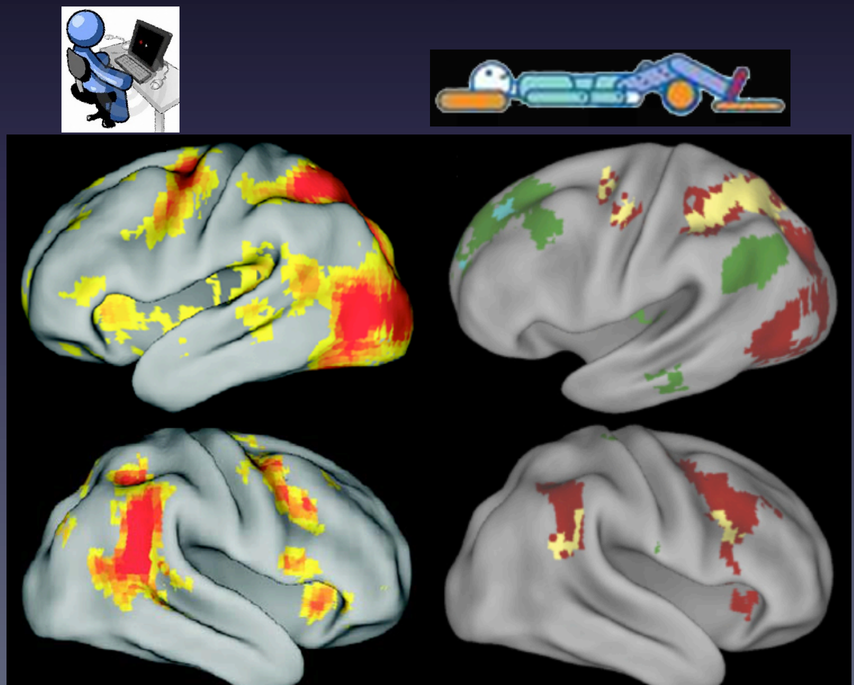
- Potential clinical applications

Signal + Noise (Linear Superposition)





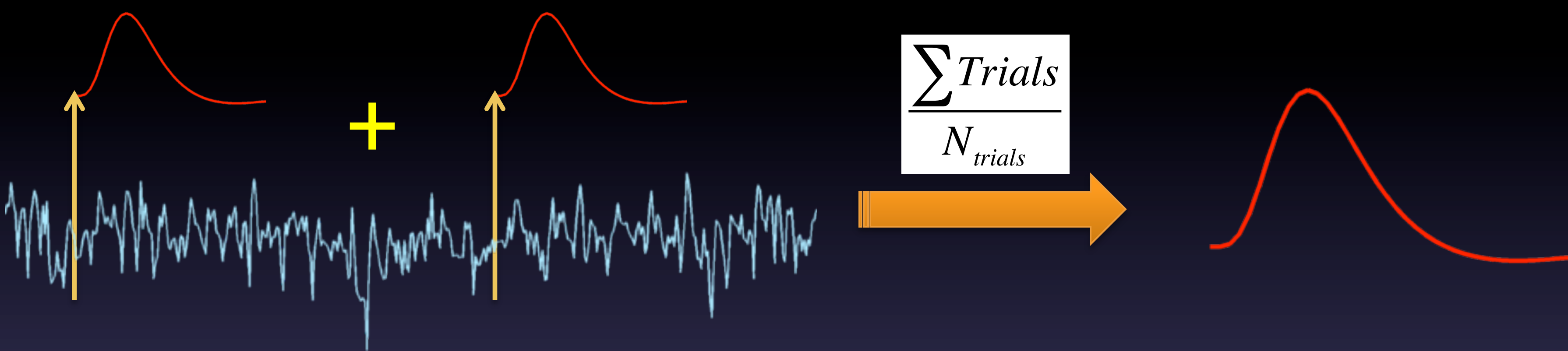
Kenet et al., Nature 2003



Biswal et al., 1995; He et al., Neuron 2007; Fox & Raichle 2007 …

Signal + Noise (Linear Superposition)

Trial-averaging:



General Linear Model:

$$Y = x_1\beta_1 + x_2\beta_2 + \ldots + x_p\beta_p + \varepsilon$$

Observation

Experimental design variables

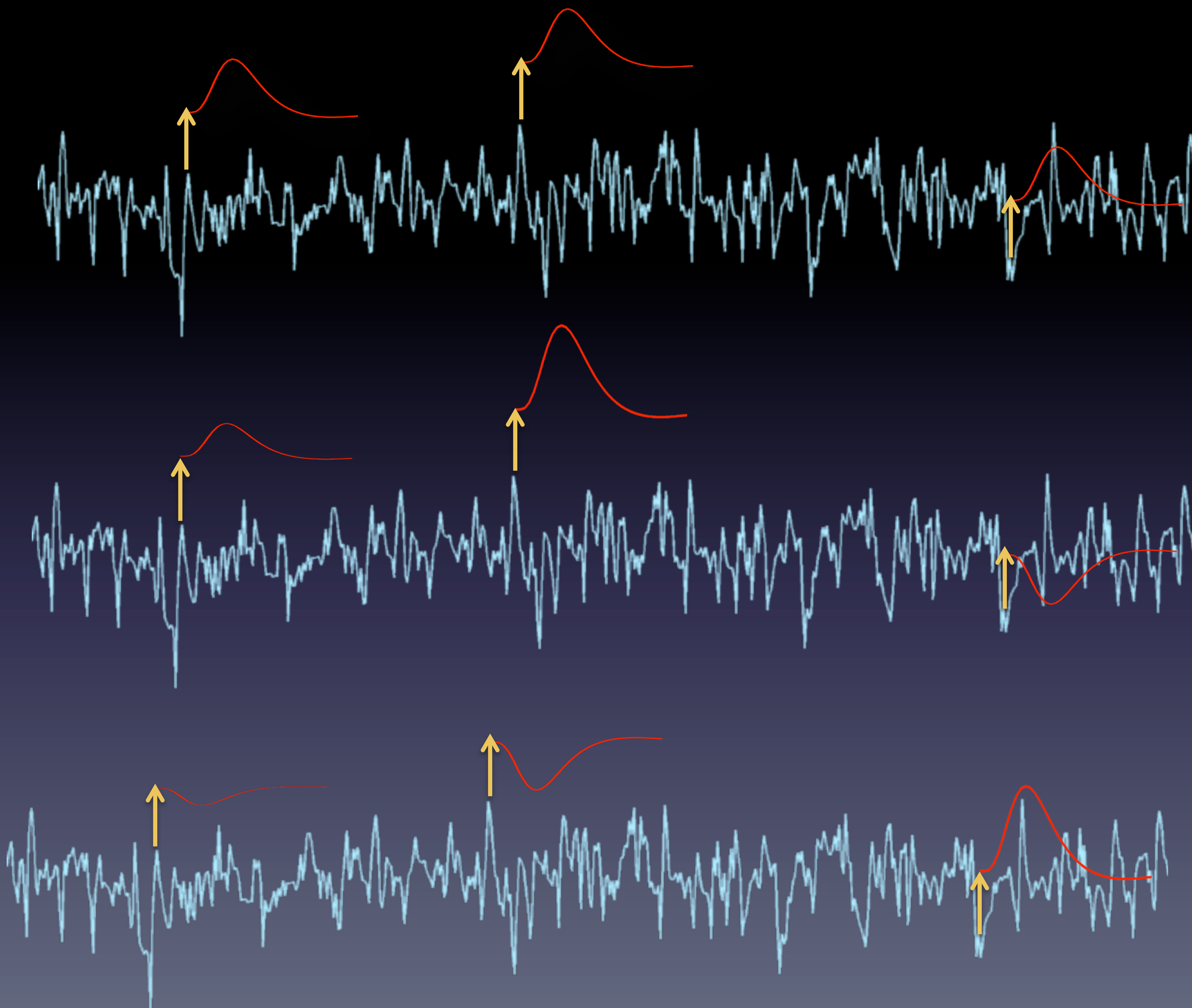
Residual

What if linear superposition is not correct?

i) Linear Superposition

ii) Positive Interaction

iii) Negative Interaction



The literature is conflicted!

Supporting linear superposition:

Dynamics of Ongoing Activity: Explanation of the Large Variability in Evoked Cortical Responses

Amos Arieli, Alexander Sterkin, Amiram Grinvald, Ad Aertsen*

Science 1996

"In spite of the large variability, evoked responses in single trials could be predicted by linear summation of the deterministic response and the preceding ongoing activity."

Voltage-sensitive dye in anesthetized cats (visual cortex)

Coherent spontaneous activity accounts for trial-to-trial variability in human evoked brain responses

Michael D Fox[1], Abraham Z Snyder[1,2], Jeffrey M Zacks[1,3] & Marcus E Raichle[1,2,4,5]

Nature Neuroscience, 2006

"coherent spontaneous fluctuations in human brain activity account for a significant fraction of the variability in measured event-related BOLD responses… spontaneous and task-related activity are linearly superimposed in the human brain."

fMRI in human subjects watching movies

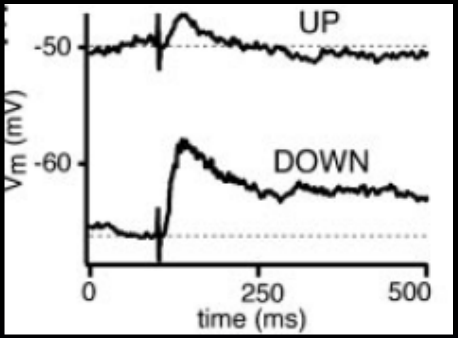
Not squaring so well with linear superposition…

Interaction of sensory responses with spontaneous depolarization in layer 2/3 barrel cortex

Carl C. H. Petersen*[†‡], Thomas T. G. Hahn*, Mayank Mehta[§¶], Amiram Grinvald[‖], and Bert Sakmann*

PNAS, 2003

Voltage-sensitive dye in anesthetized and awake rats (barrel cortex)



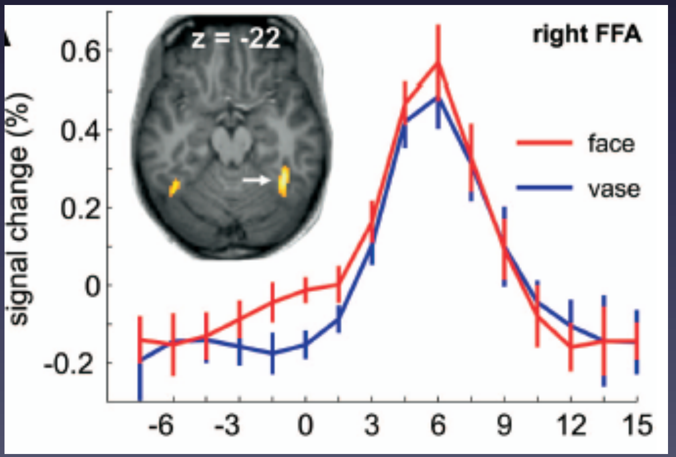
“Surprisingly, unlike in the anesthetized cat… here we find that both sensory-evoked postsynaptic potentials (PSPs) and sensory-evoked action potentials (APs) are suppressed by (higher) ongoing spontaneous activity.”

Spontaneous local variations in ongoing neural activity bias perceptual decisions

Guido Hesselmann[†‡§¶], Christian A. Kell[‖], Evelyn Eger[†‡§], and Andreas Kleinschmidt[†‡§]

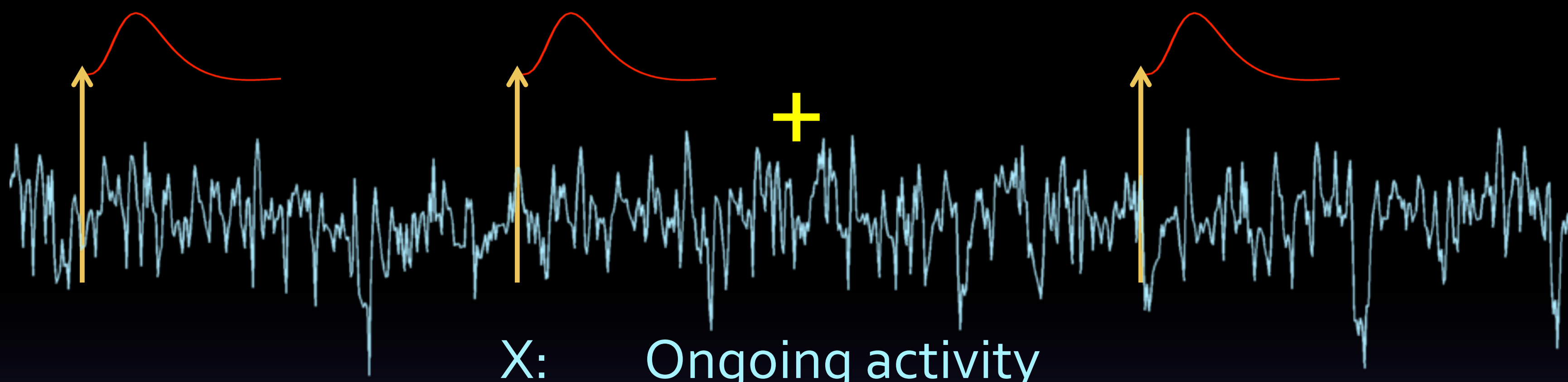
PNAS, 2008

fMRI in human subjects performing a task



“That the difference in activity between vase and faces trials changes over peristimulus time is consistent with a modulation of evoked responses by preceding levels of baseline activity and suggests an interaction between baseline activity and the evoked response.”

Testing linear-superposition



X: Ongoing activity

Y: Task-evoked activity

X+Y: Recorded signal

Linear Superposition: $r_{X,Y} = 0$;

Stereotypical task-evoked activity: $\sigma^2_Y = 0$.

One observable, two unknowns!!!

The law of variance sum:

$$\sigma^2_{X+Y} = \sigma^2_X + \sigma^2_Y + 2r_{X,Y}\,\sigma_X\,\sigma_Y$$

$$\sigma^2_{X+Y} = \sigma^2_X + \sigma^2_Y + 2r_{X,Y}\,\sigma_X\,\sigma_Y$$

Recorded (under task) — Ongoing — Evoked

- Linear Superposition: $r_{X,Y} = 0$

$$\sigma^2_{X+Y} = \sigma^2_X + \sigma^2_Y$$

  – Prediction: $\sigma^2_{X+Y} \geq \sigma^2_X$ (equal sign in the limit of $\sigma^2_Y = 0$)

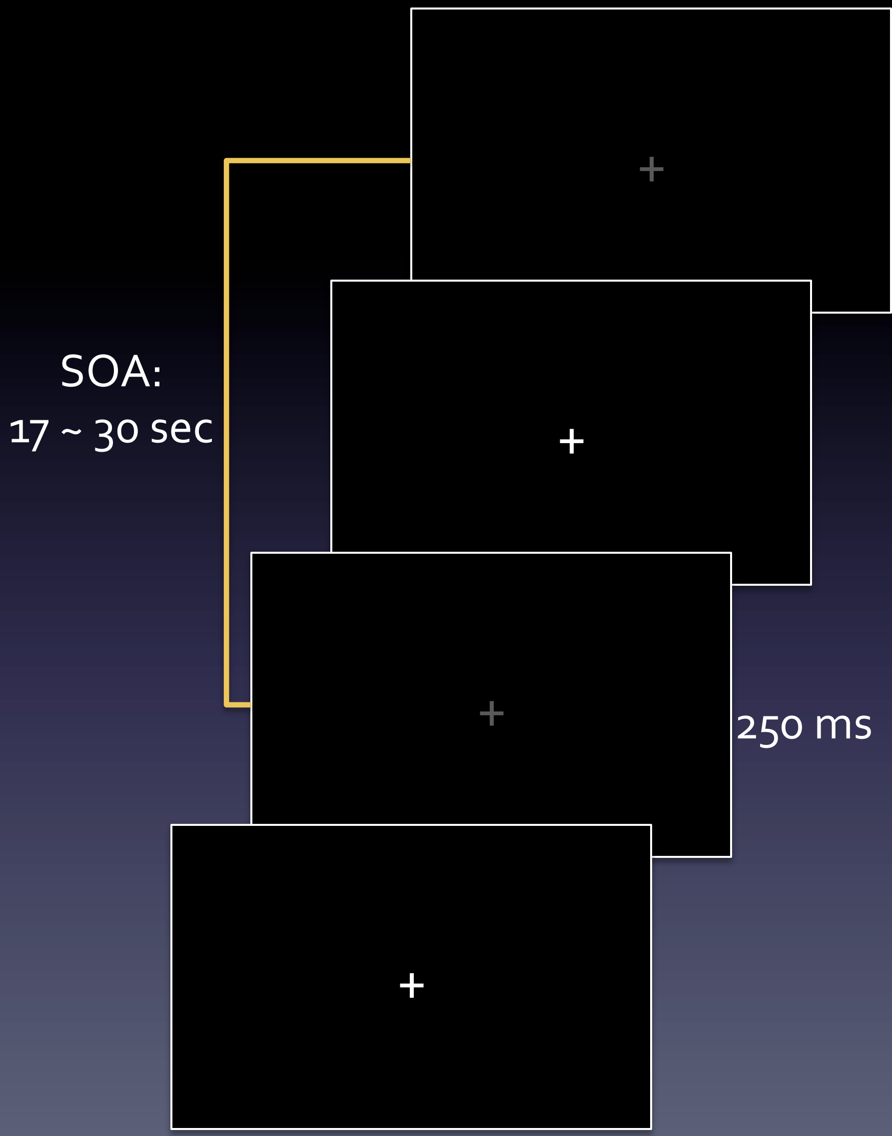
- Positive Interaction: $r_{X,Y} > 0$
  – Prediction: $\sigma^2_{X+Y} \geq \sigma^2_X$ (equal sign in the limit of $\sigma^2_Y = 0$)

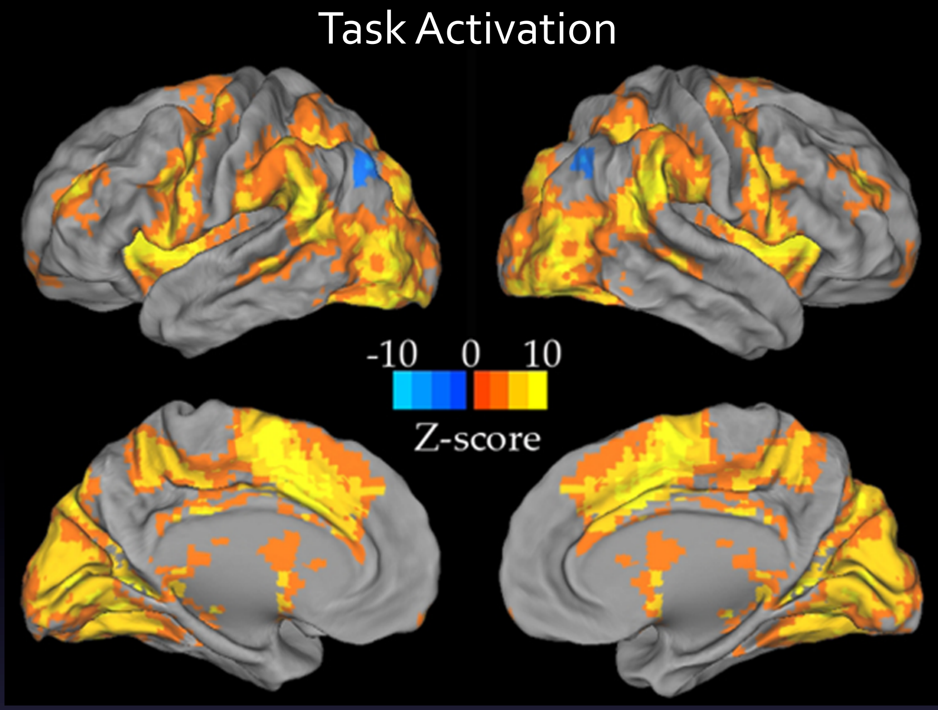
- Negative Interaction: $r_{X,Y} < 0$
  – Prediction: $\sigma^2_{X+Y} > \sigma^2_X$, if $-\sigma_Y/2\sigma_X < r_{X,Y} < 0$

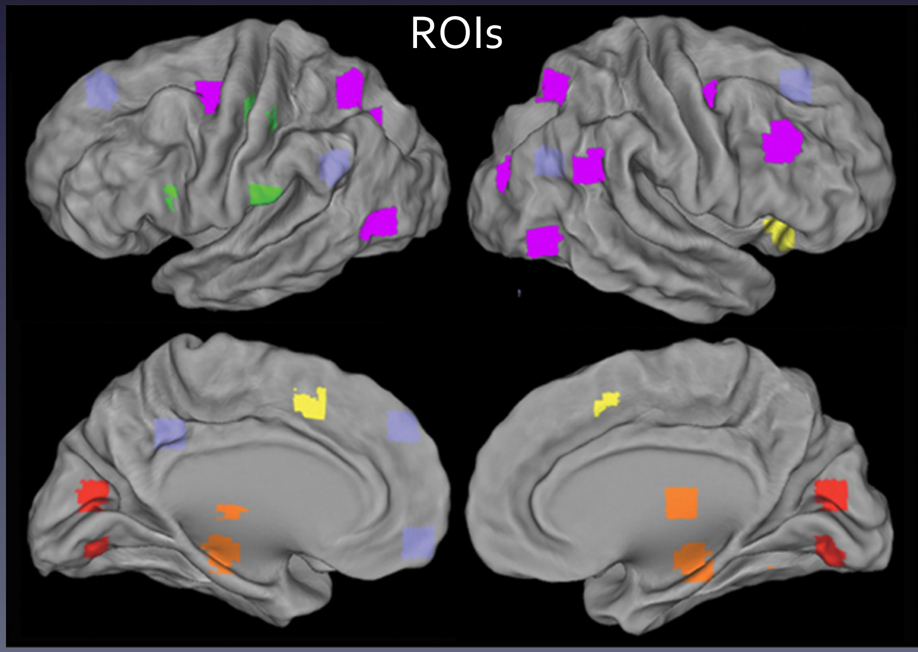
  $\sigma^2_{X+Y} < \sigma^2_X$, if $r_{X,Y} < -\sigma_Y/2\sigma_X < 0$

  $\sigma^2_{X+Y} = \sigma^2_X$, if $r_{X,Y} = -\sigma_Y/2\sigma_X$

Task Design



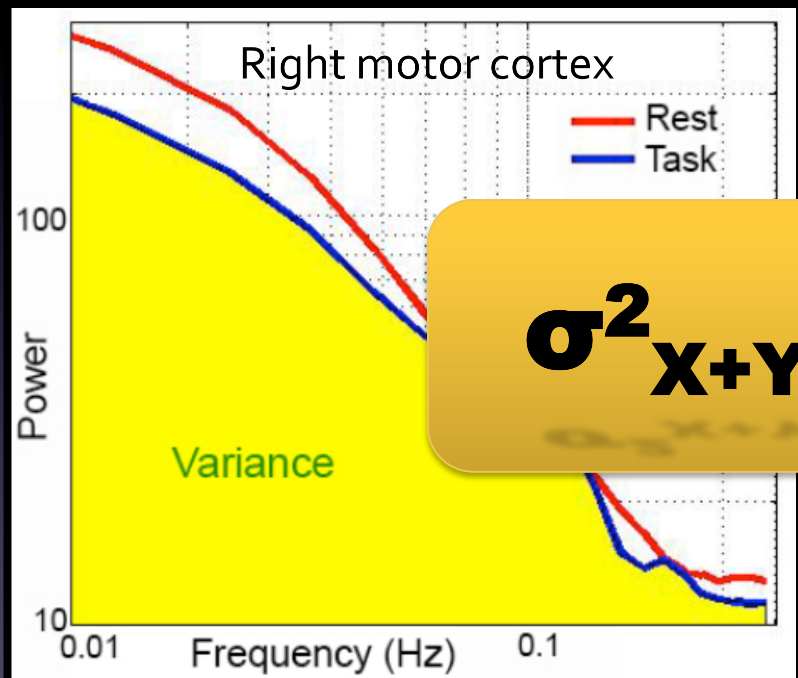


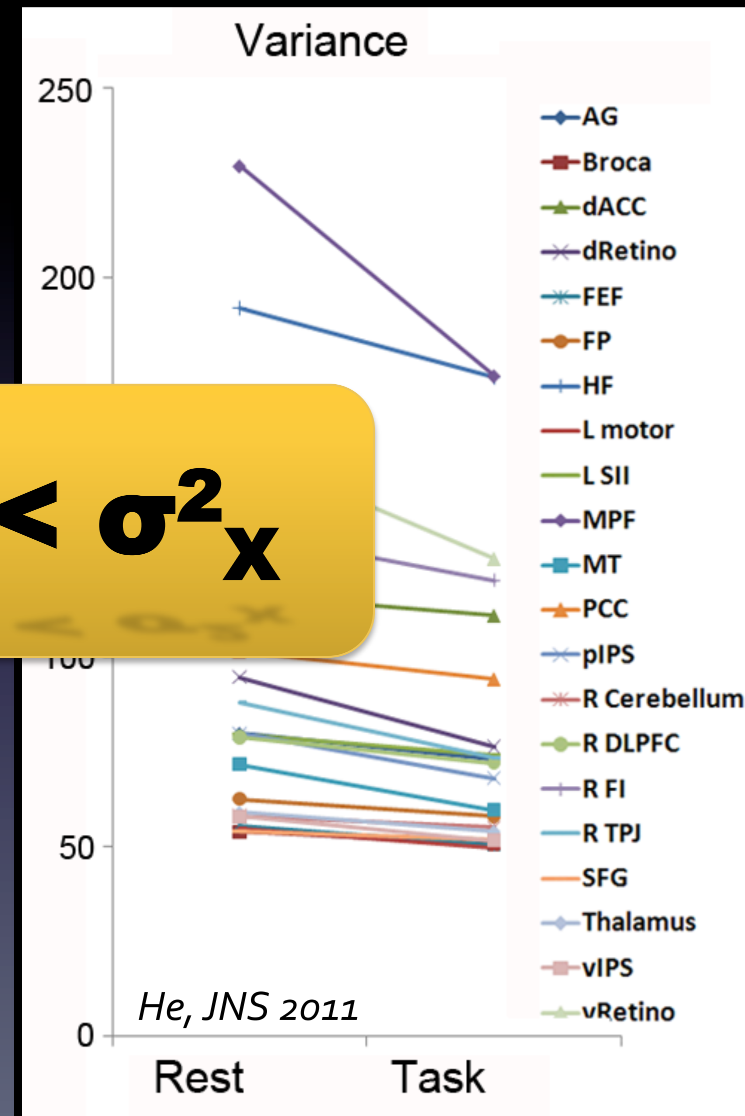


Fox et al., Neuron 2007; He et al., Neuron 2010

σ^2_{X+Y} vs. σ^2_X

Test 1: Variance of brain activity during task (X+Y) vs. rest (X)

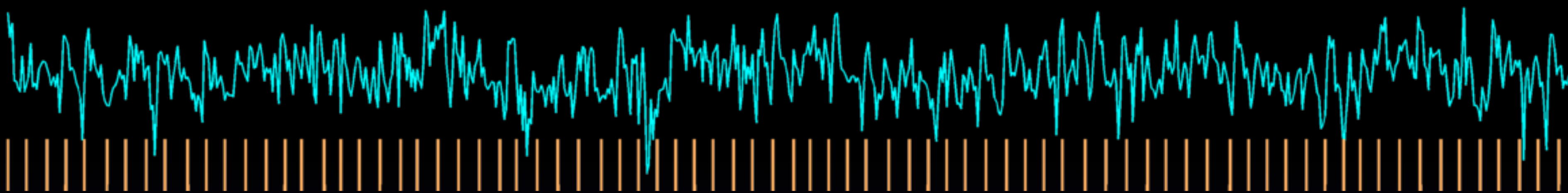




$$\sigma^2_{X+Y} < \sigma^2_X$$

σ^2_{X+Y} vs. σ^2_X

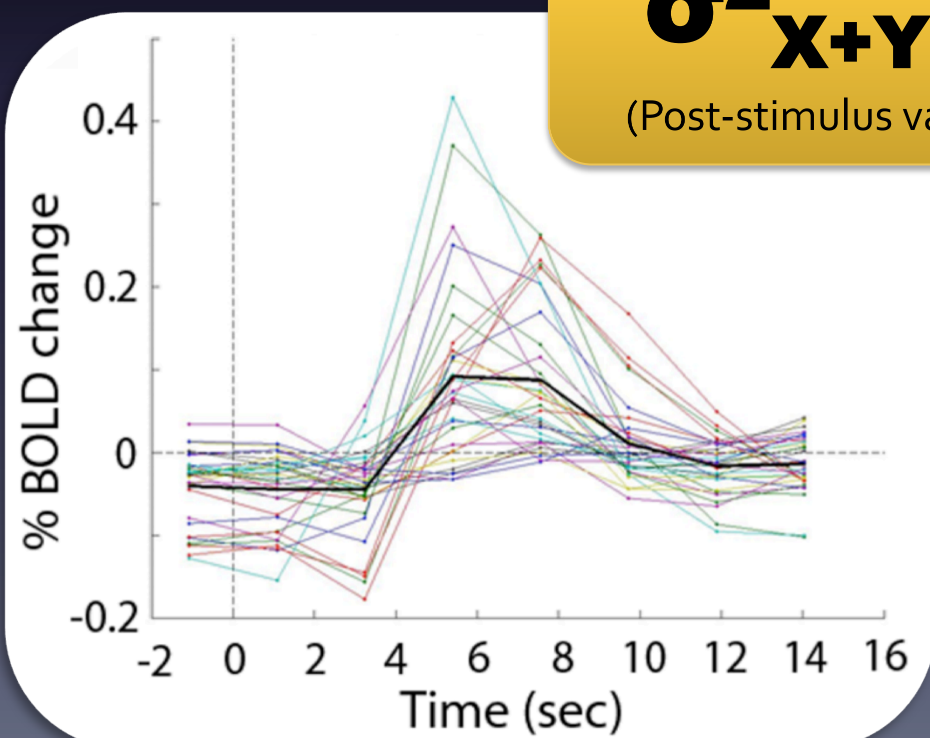
Test 2: Variance of post-stimulus (X+Y) vs. pre-stimulus (X) activity

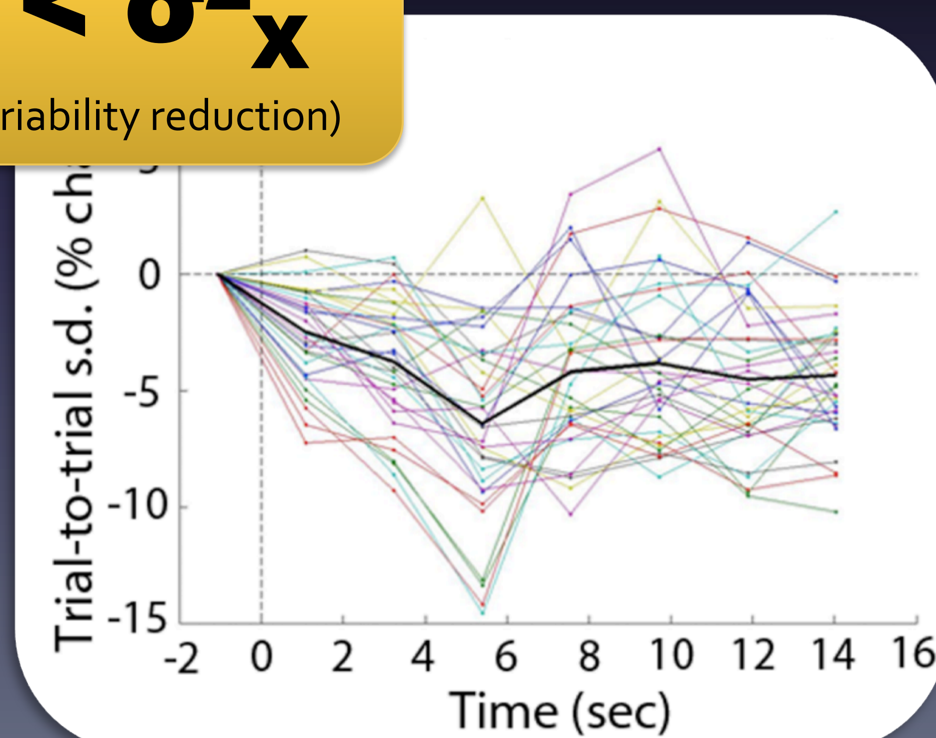


single subj., ~27 min experiment, 80 trials

$$\boldsymbol{\sigma^2_{X+Y} < \sigma^2_X}$$

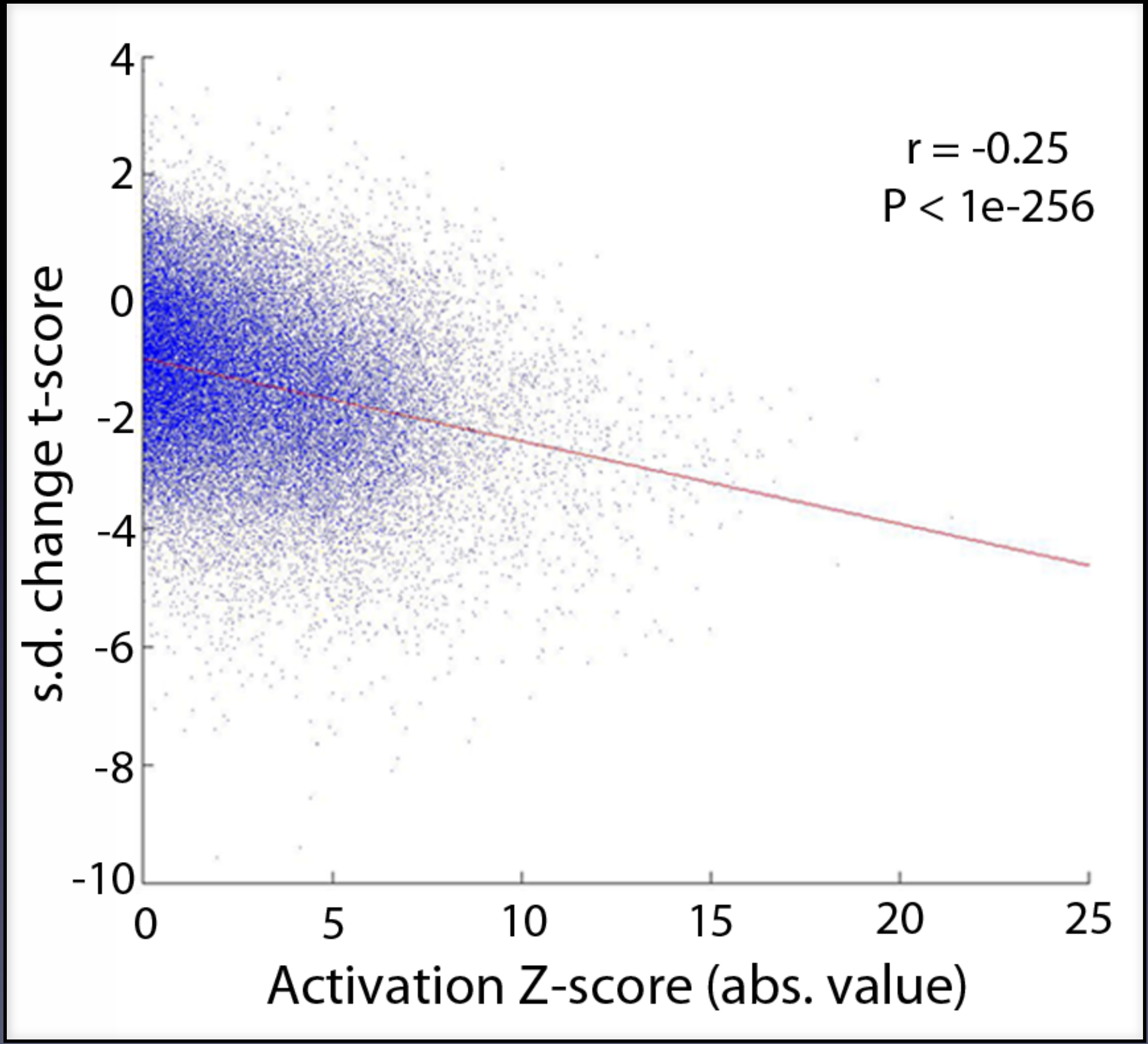
(Post-stimulus variability reduction)





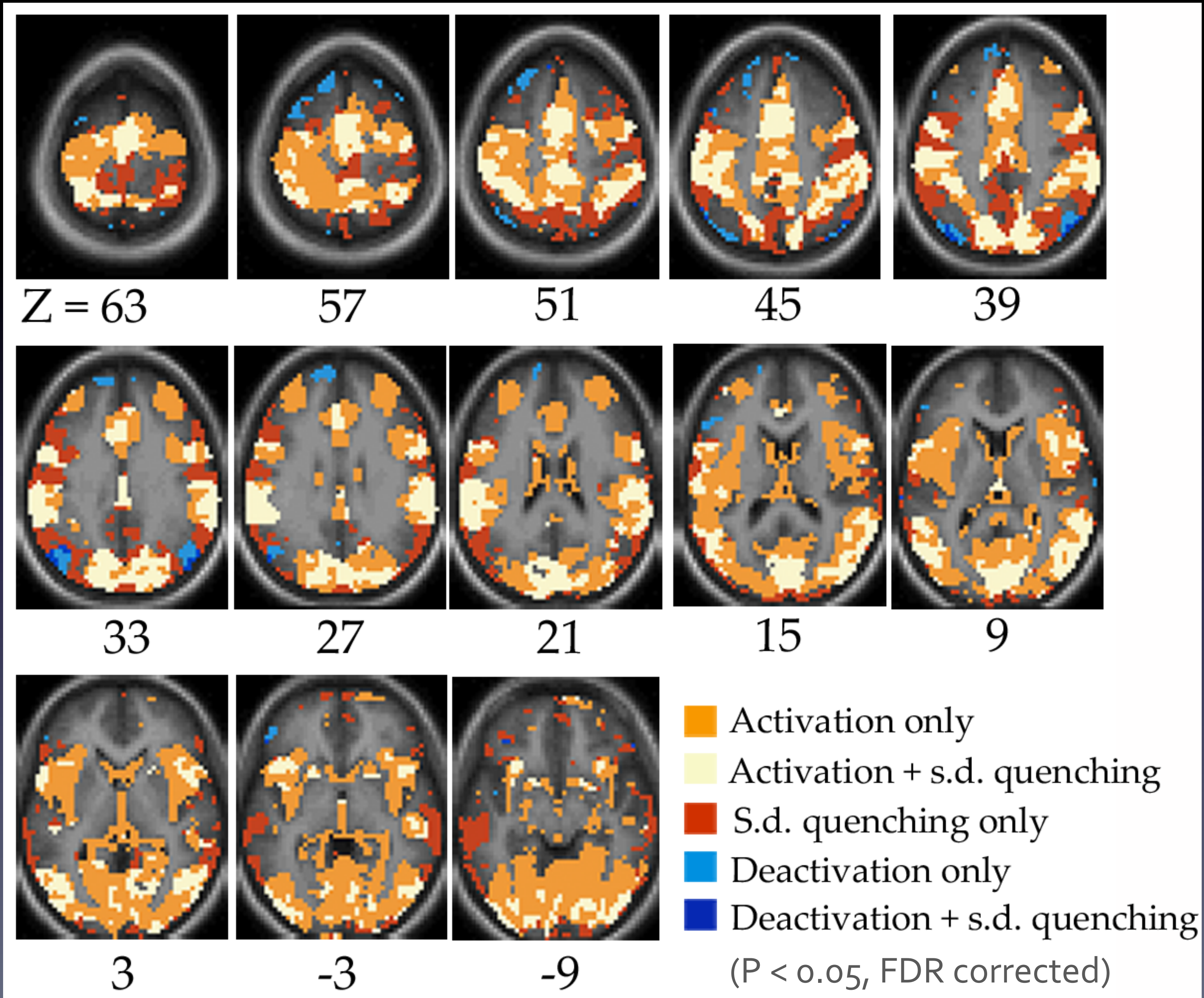
Whole-brain voxel-wise analysis

Trial-to-trial Variability

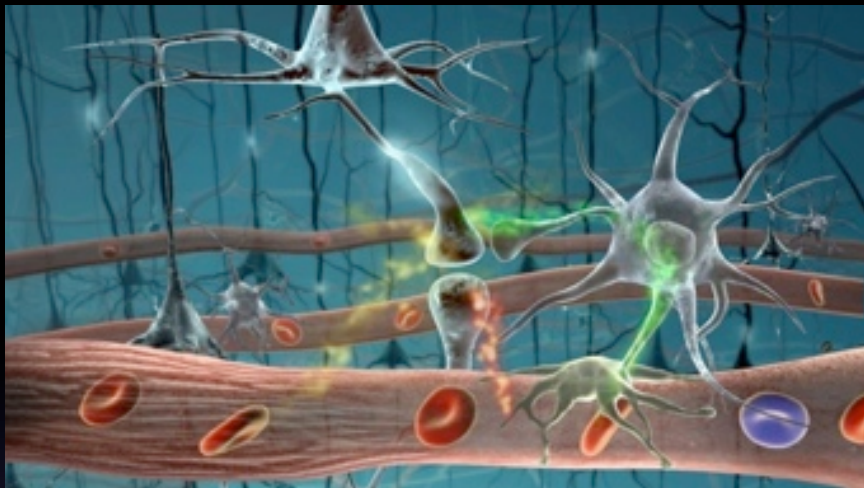


Trial-averaged Activity

Whole-brain voxel-wise analysis



Could it all be hemodynamic?



Stimuli → Neural Activity → CBF → BOLD

nonlinearity (Stimuli → Neural Activity)

nonlinearity (CBF → BOLD)

Friston et al., MRM 1998
Miller… Buxton, HBM 2001

How to test? Assuming linear-superposition in the neural activity, can hemodynamic response introduce variability reduction?

Spontaneous: Neural activity → CBF → BOLD (Balloon Model)

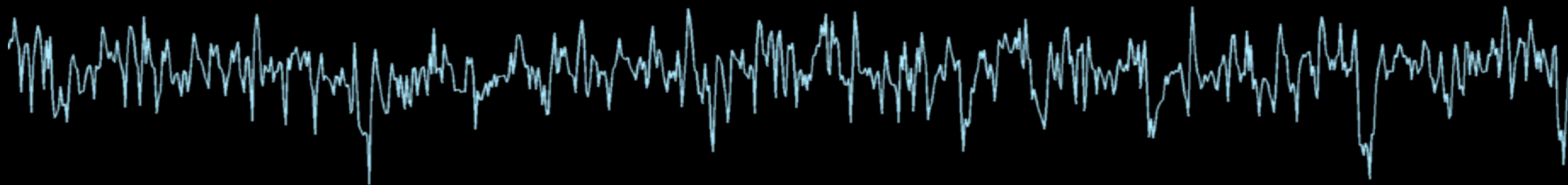
\+ +

Evoked: Neural activity → CBF → BOLD (Balloon Model)

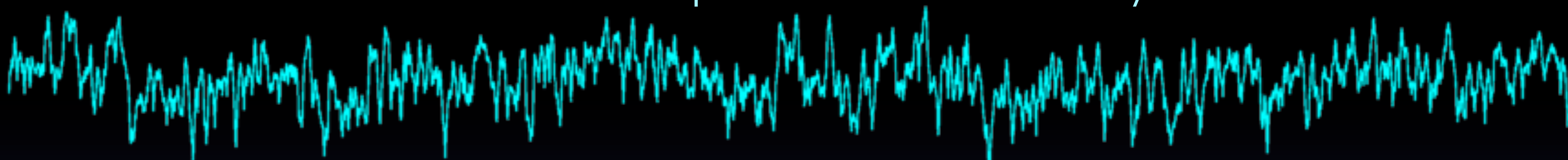
= =

Neural activity → CBF → BOLD (Balloon Model) ?

Recorded resting-state fMRI signal

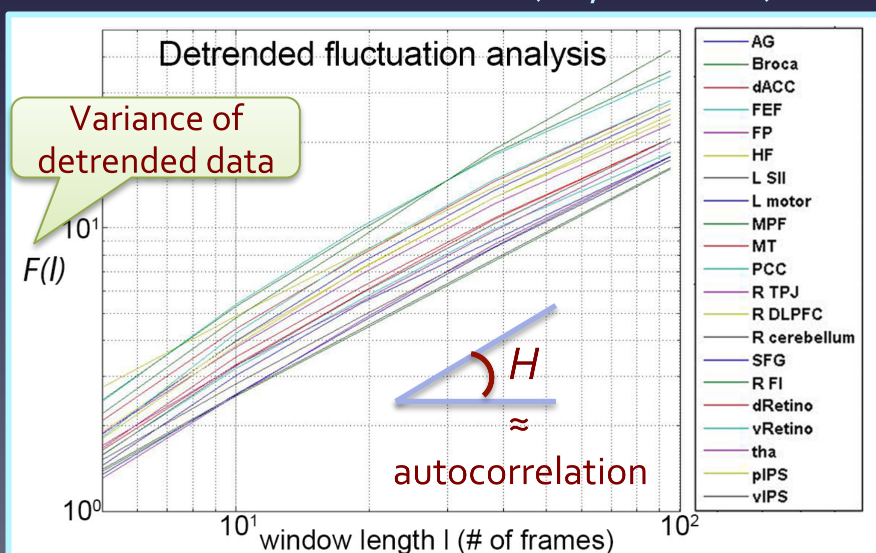


Simulated spontaneous BOLD activity

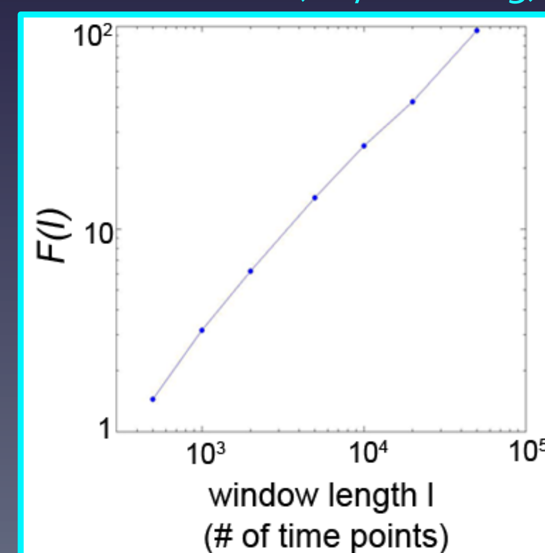


	Range (% change)	SD (% change)	Hurst exponent *H*
Empirical	30.1	4.45	0.84
Simulation	30.9	4.41	0.83

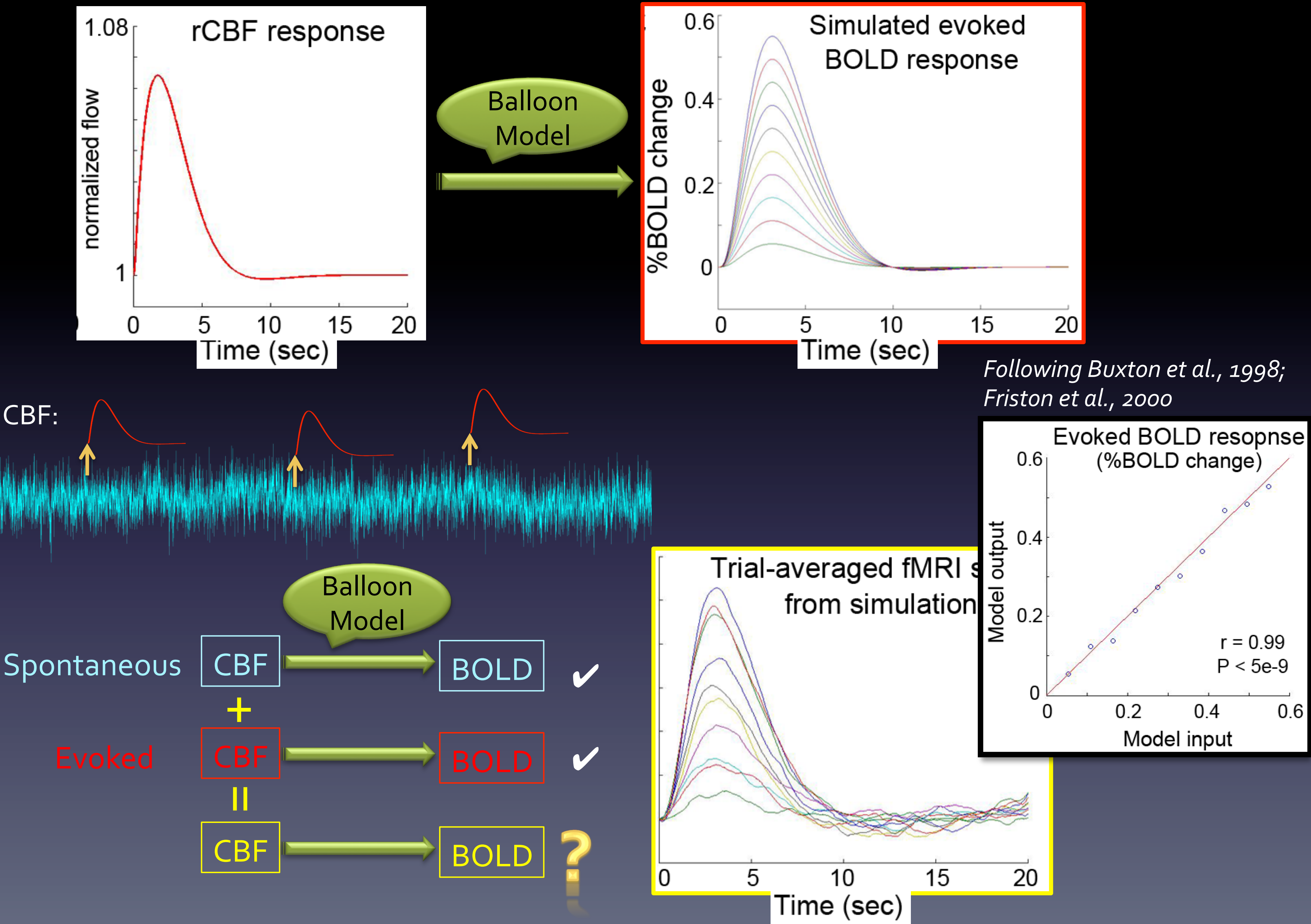
Recorded fMRI data *(He, JNS 2011)*



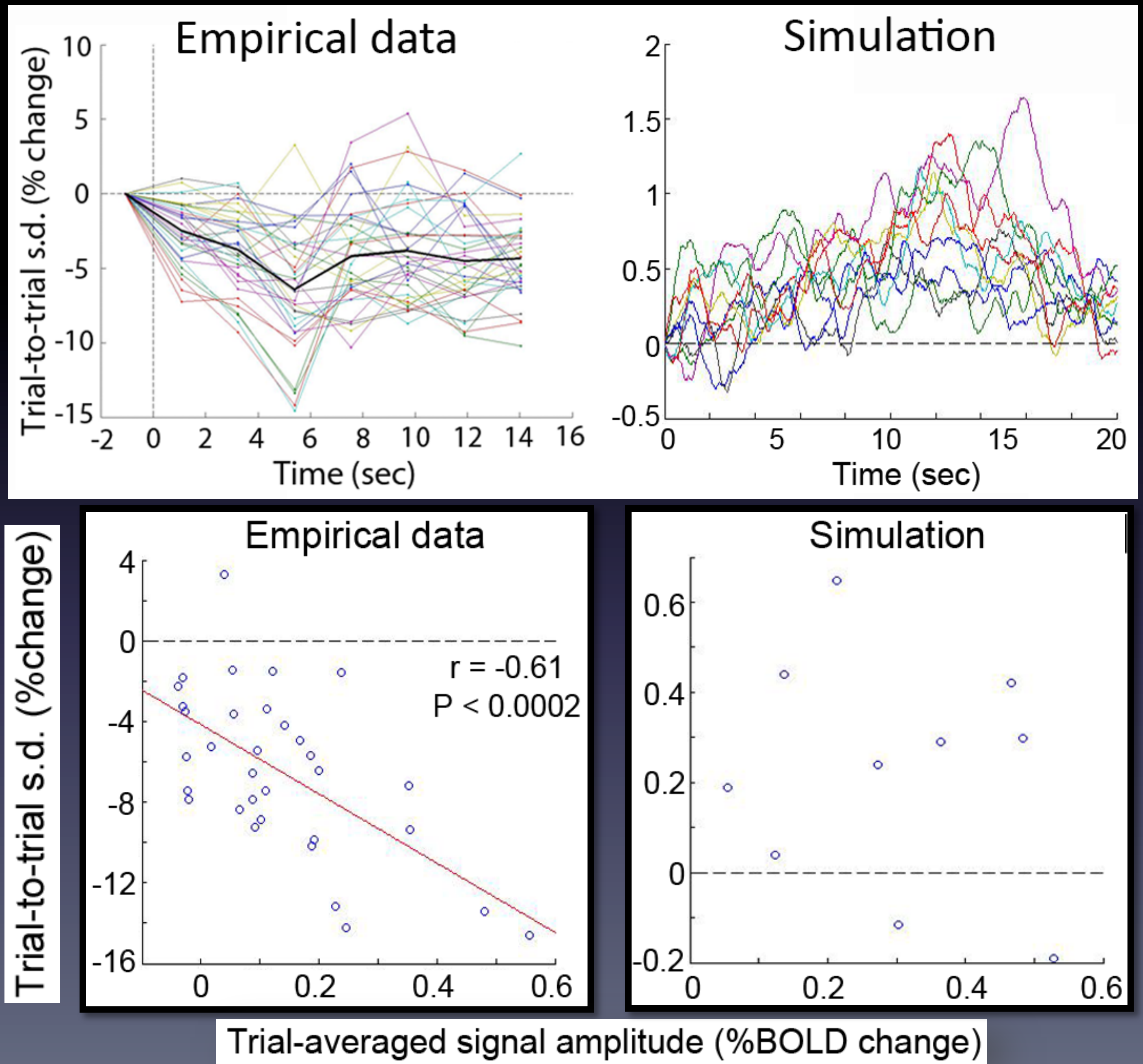
Simulated data *(He, JNS 2013)*



Simulated evoked BOLD activity



HRF nonlinearity cannot cause variability reduction



Interim Summary

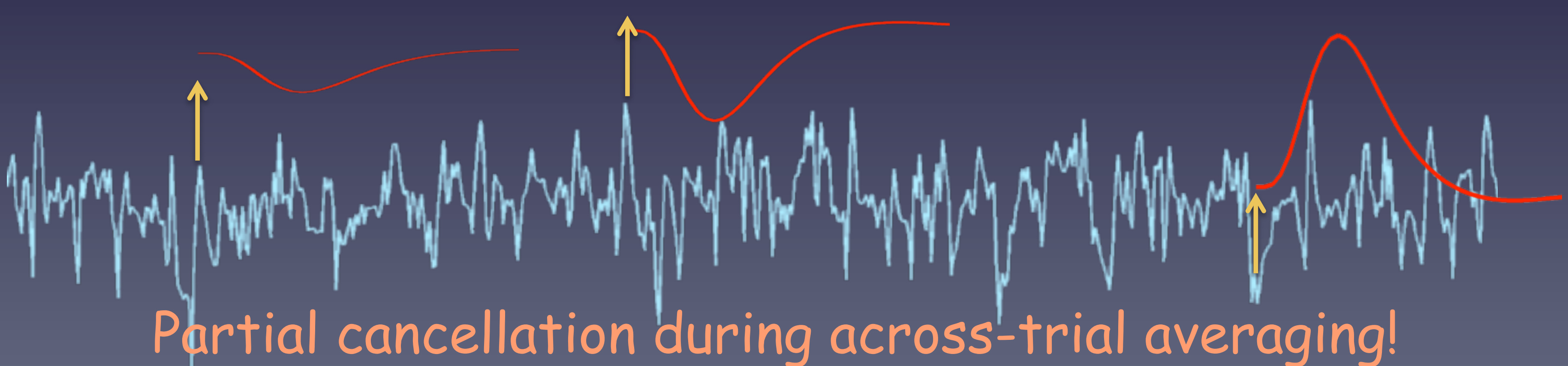
Observations:

- Temporal variance — Task < Rest
- Across-trial variability — Post-stimulus < Pre-stimulus

If we assume there exists separate ongoing and evoked activity and that ongoing activity is (mean- and variance-) stationary:

Given the Law of Variance Sum,

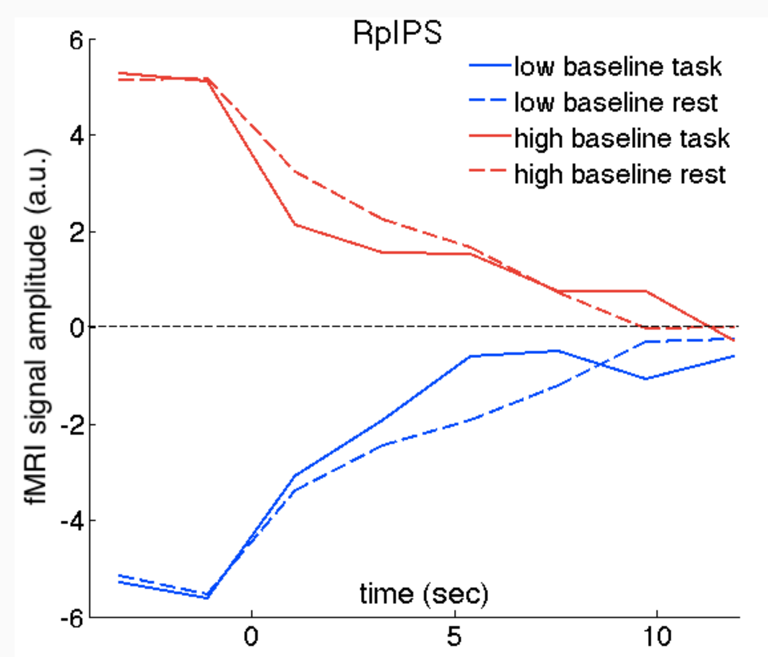
Ongoing and evoked activity must negatively interact.

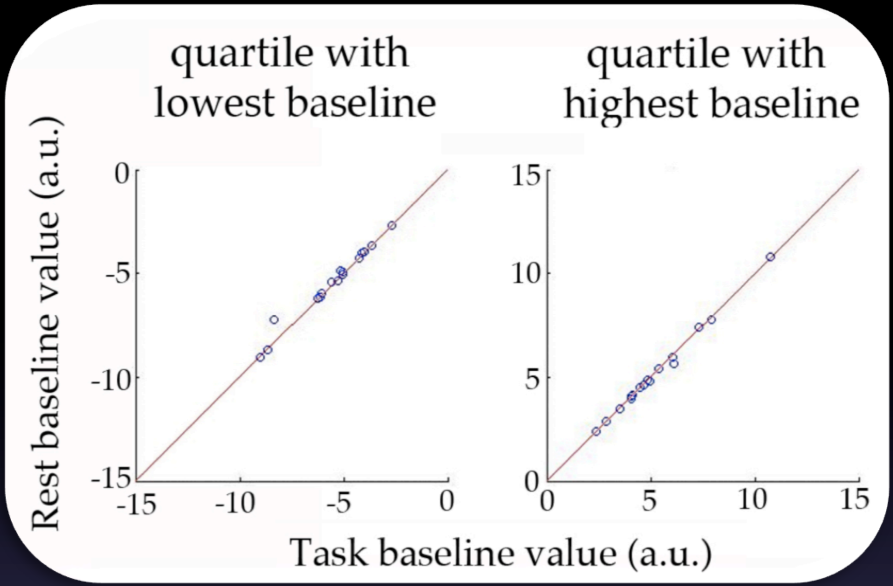


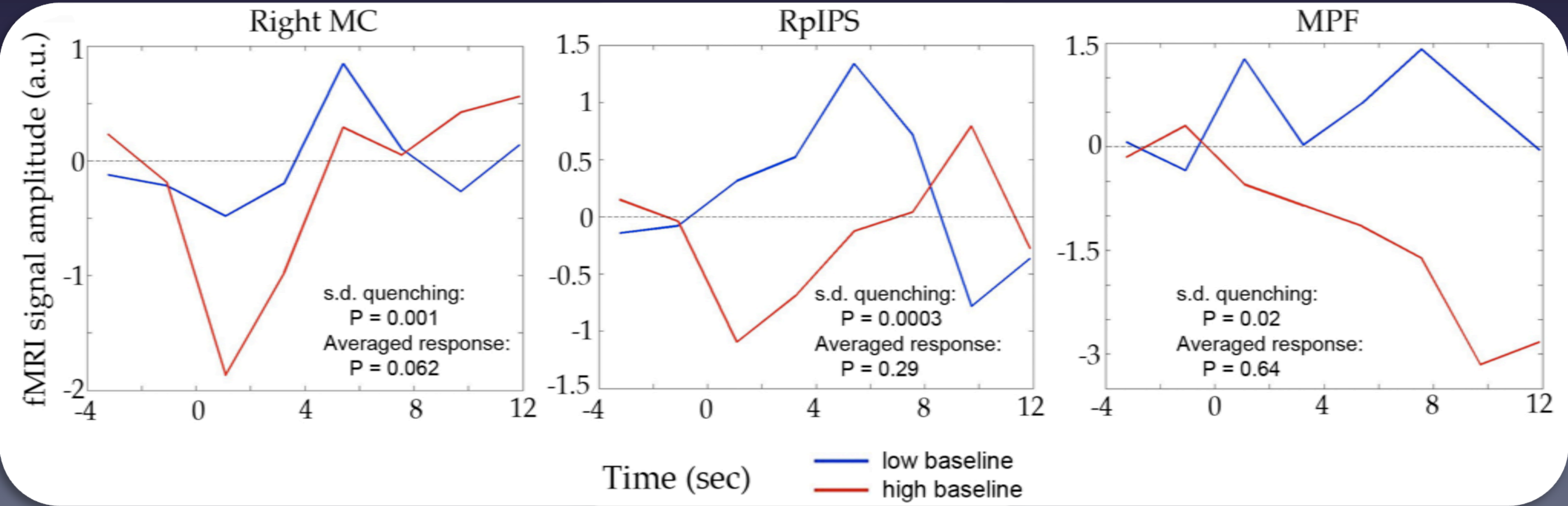
Partial cancellation during across-trial averaging!

He, JNS 2013

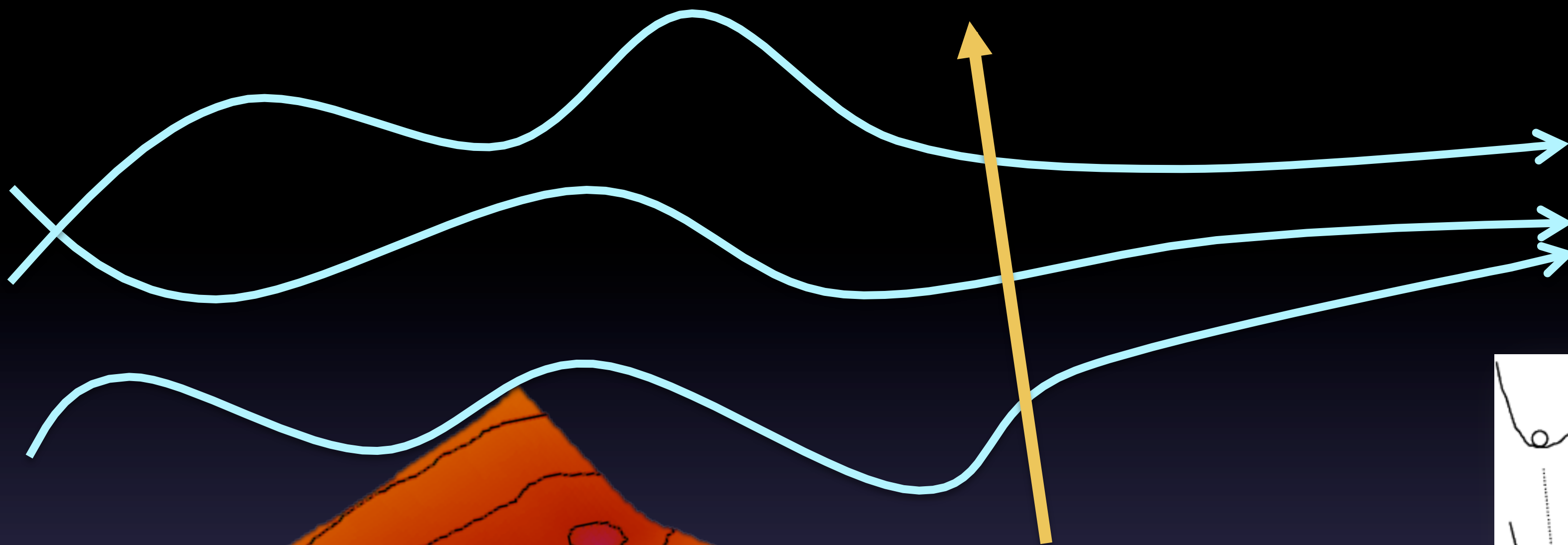
Partial cancellation during across-trial averaging

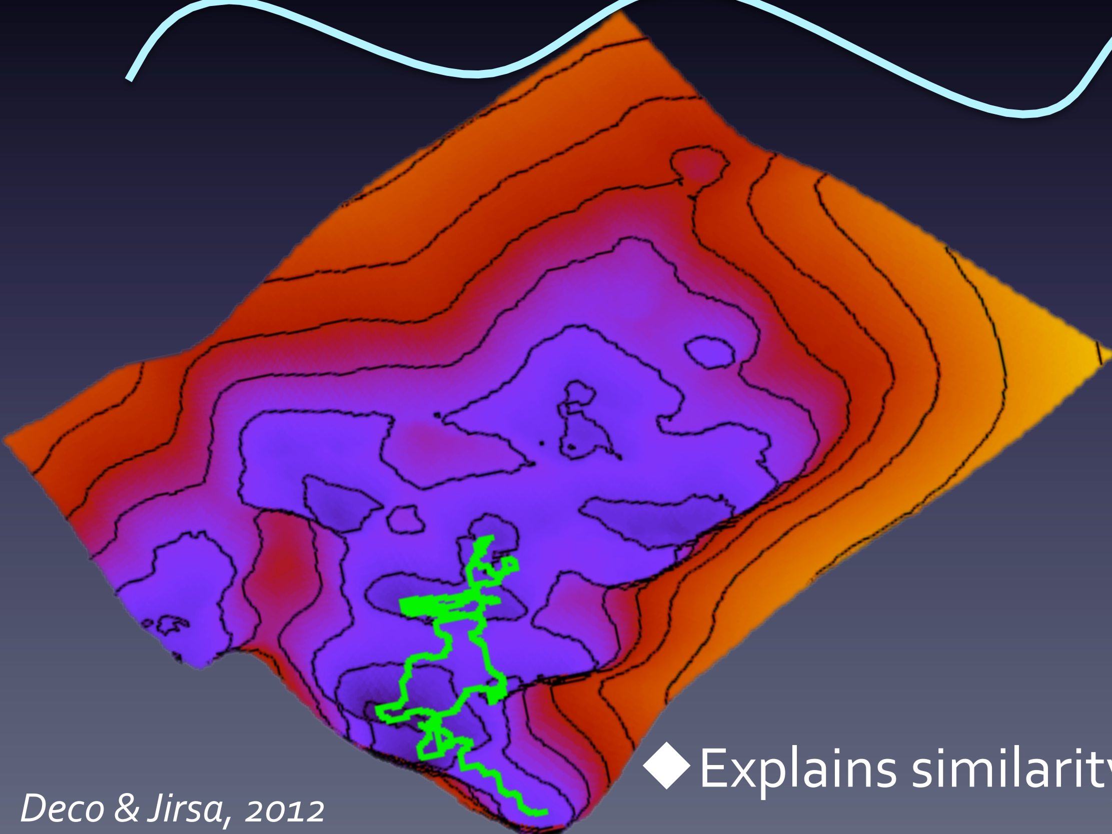


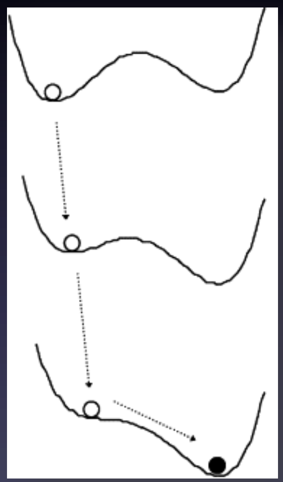




Is trajectory-based idea more parsimonious?



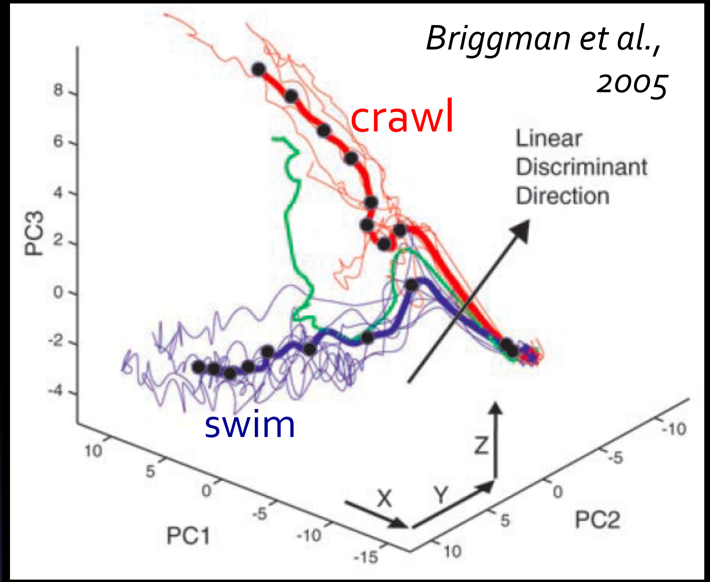




- Variability reduction
- Negative interaction
- Explains similarity between RSN and task-systems

Deco & Jirsa, 2012

Trajectory-based processing

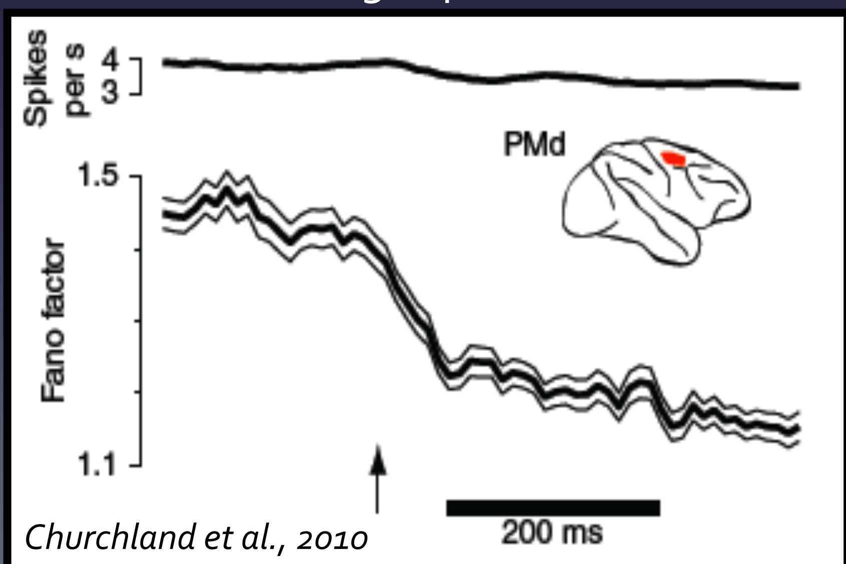


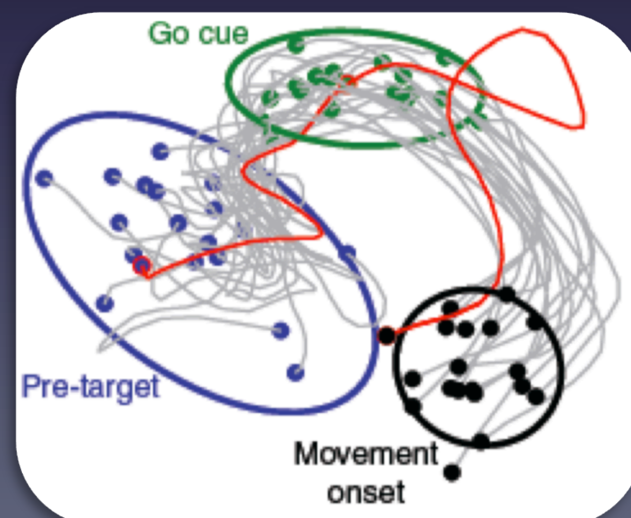
"... information is encoded in evolving neural trajectories. ... computation is in the voyage through state space as opposed to the destination."

"The response of a population of neurons in a network is determined not only by the characteristics of the external stimulus but also by the dynamic changes in the internal state of the network."

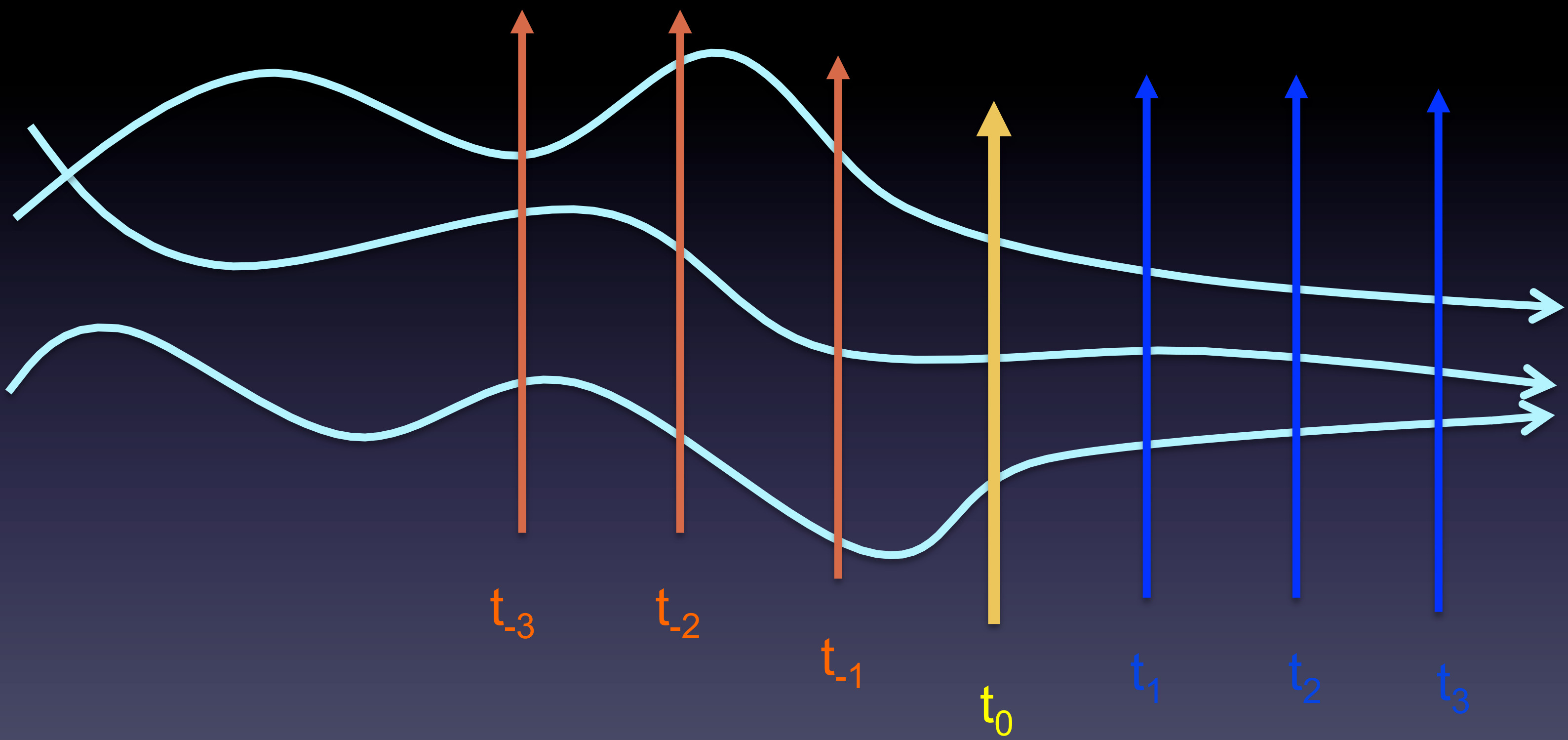
(Buonomano& Maass, 2009)

Neuronal firing in premotor cortex

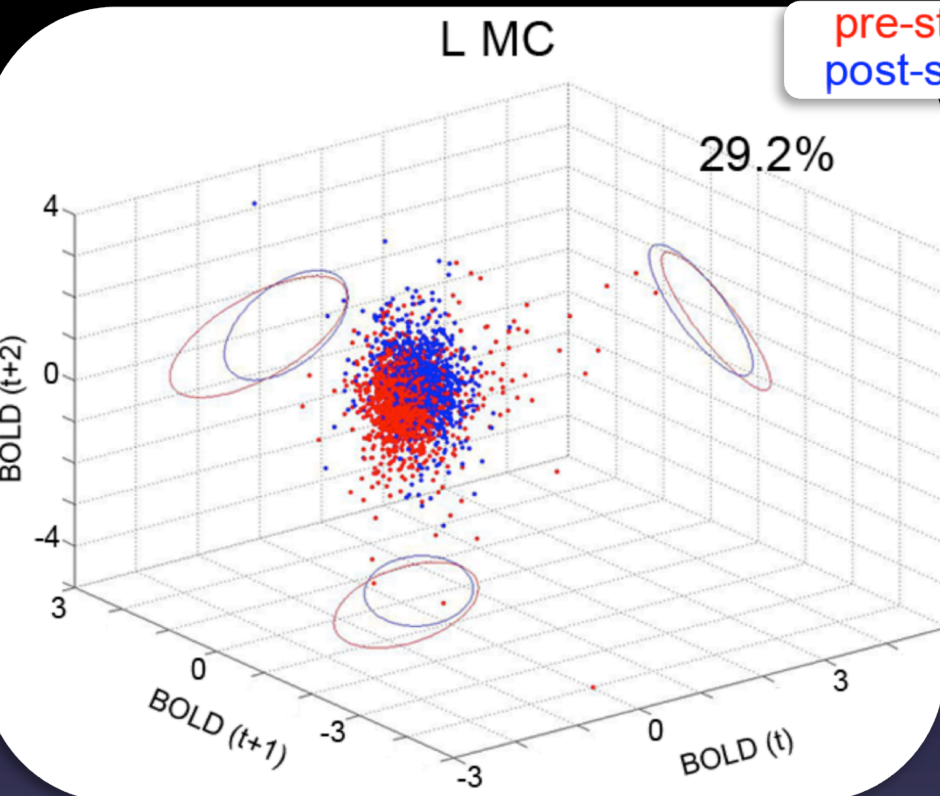


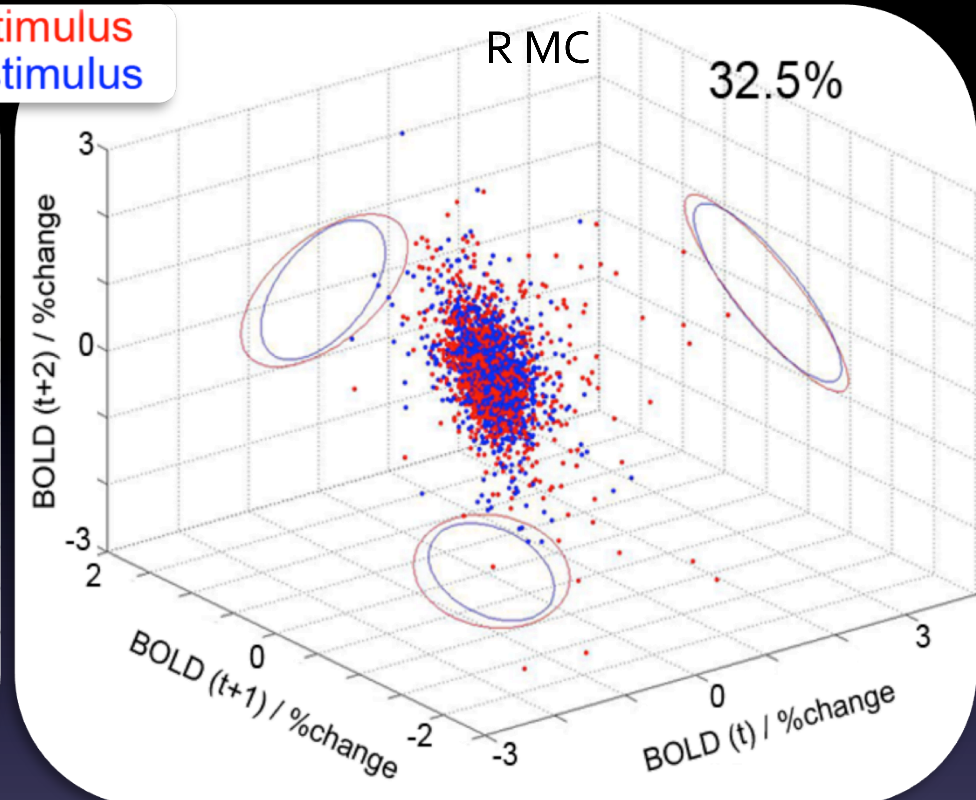


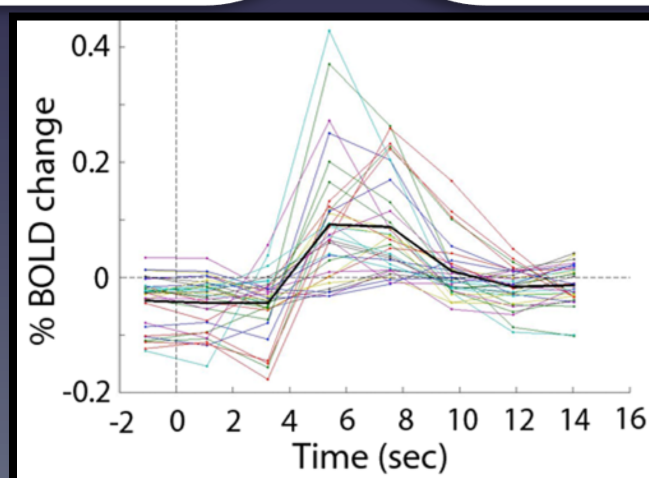
Assessment of cortical state space



Shrinking of cortical state-space



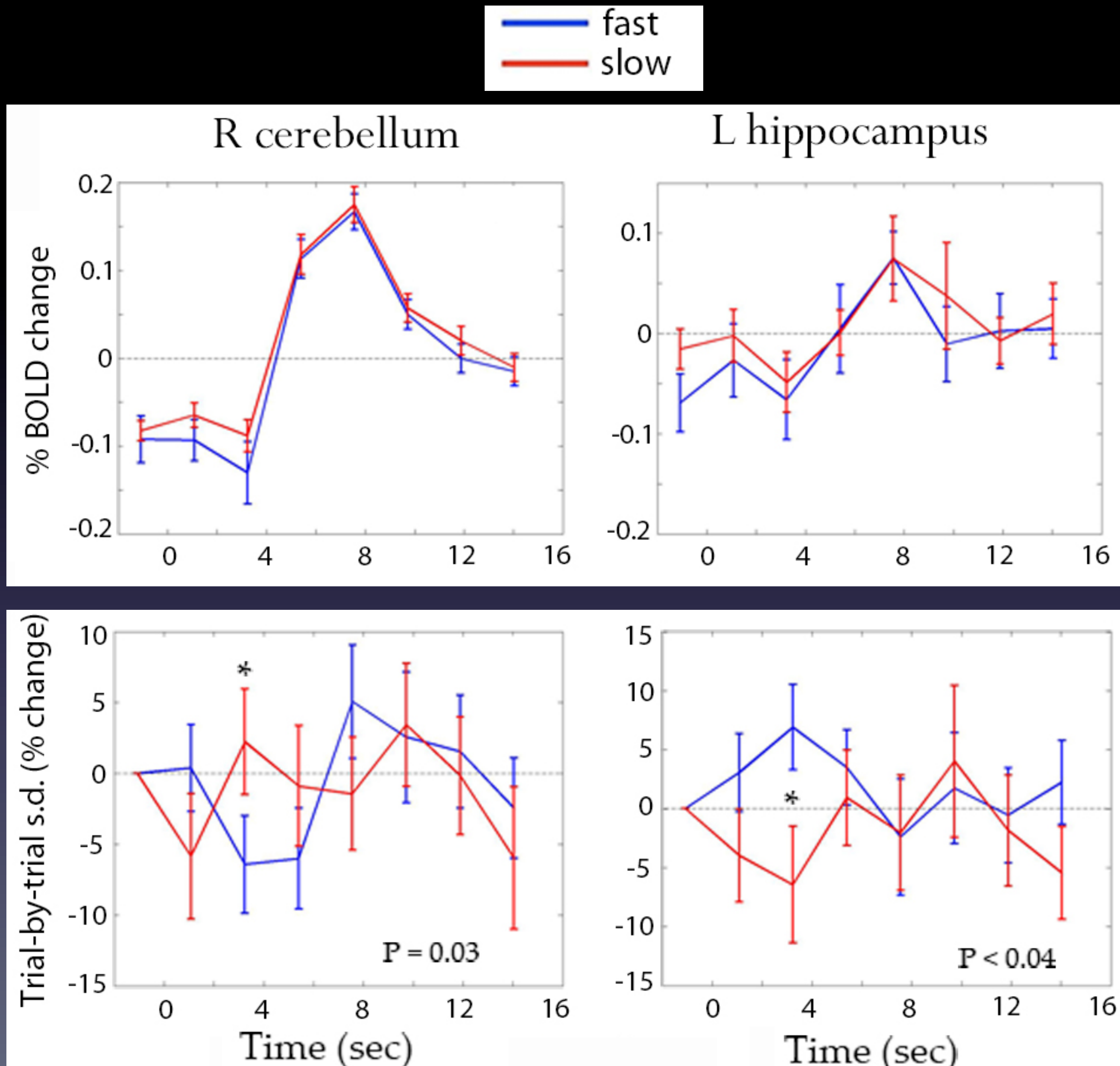




Trial-averaged activity
LMC: 0.4%
RMC: 0.07%

He, JNS 2013

Across-trial variability correlates with behavior



He, JNS 2013

Interim Summary

- Spatial patterns of across-trial variability and trial-averaged response are dissociable.
- Variability reduction contains behaviorally relevant information not present in trial-averaged response.

→ Reevaluation of which brain regions are involved in which functions…

- Trajectory-based processing framework is more parsimonious and potentially closer to reality.

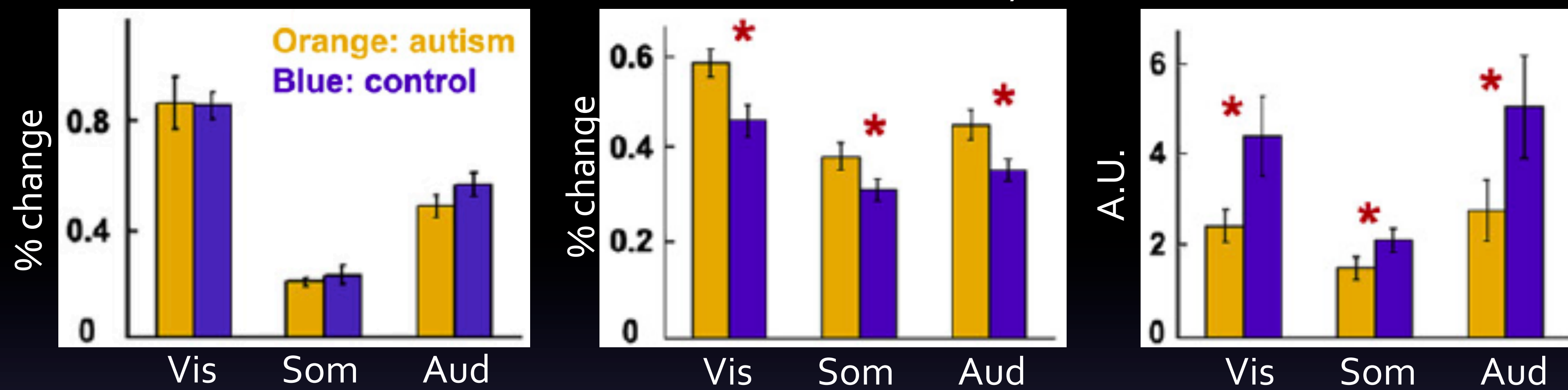
Q: How does the brain distinguish between ongoing and evoked activity?

- The brain processes incoming sensory stimuli in a strongly initial-state-dependent manner.

Potential clinical applications - variability

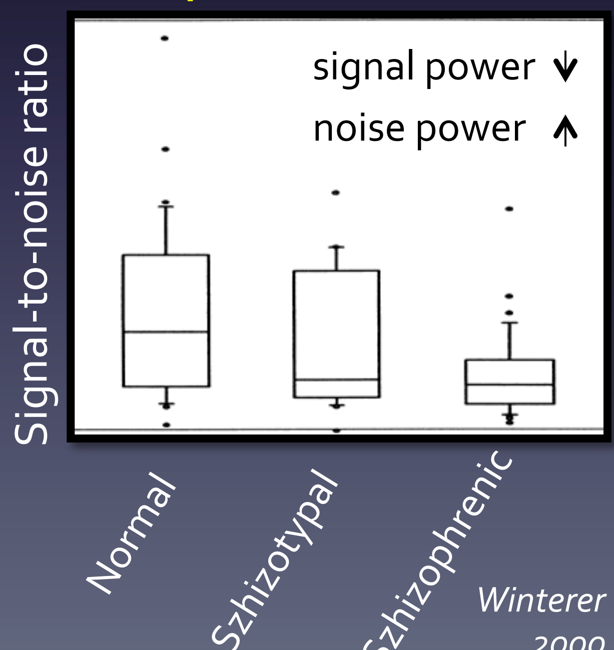
Autism

Trial-averaged activity — Across-trial variability — Signal-to-noise ratio



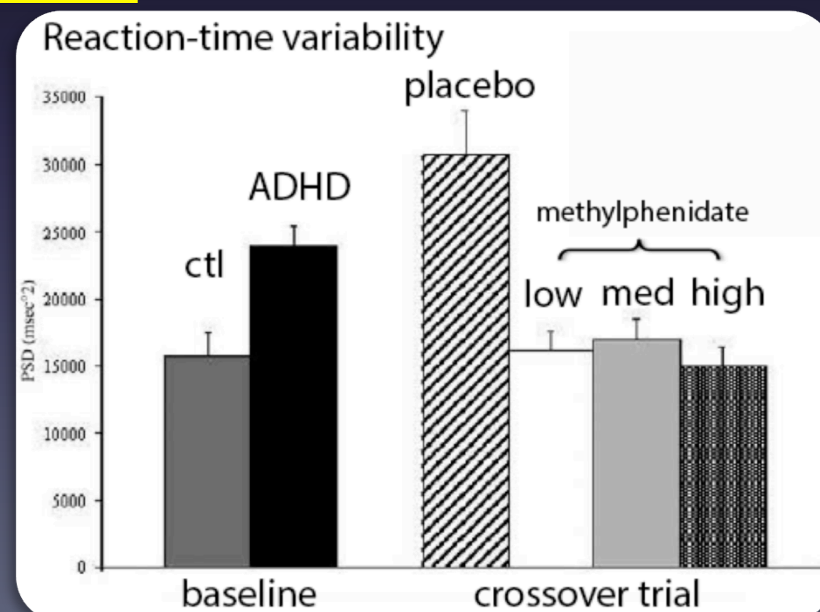
Dinstein et al., 2012 (fMRI)

Schizophrenia



Winterer et al., 2000 (EEG)

ADHD



Castellanos et al., 2005

Overall conclusions

- Prevalent variability reduction observed in fMRI and ECoG data under a simple visual detection task contradicts the widely assumed "linear superposition" model.
- If we assume that ongoing and evoked activity sum to give rise to the recorded brain signal, then they must negatively interact to produce variability reduction.
- An alternative and more parsimonious framework is that cortical activity trajectory carries information processing in itself; and that the distinction between ongoing and evoked activity under task context is artificial.
- Variability reduction contains behaviorally relevant information not present in trial-averaged response, opening up a new avenue for cognitive and clinical neuroscience.

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